CURRENT APPLICATIONS AND PERSPECTIVES OF ARTIFICIAL INTELLIGENCE IN ONCOLOGY

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ABSTRACT

With the exponential growth in Artificial Intelligence (AI) in recent years, increasing applications have been observed across various fields, with oncology - the study of cancer - being no exception. The study of mathematical oncology involves the modelling and prediction of cancer growth and treatment response with the use of mathematical models. This appears to be a promising area for incorporating AI and machine learning (ML), but there exist many limitations to be analysed. This article focuses on the current applications of AI in oncology, alongside its limitations and future advances. The applications of AI in cancer research across various areas such as mathematical oncology as well as diagnosis, prognosis, treatment, and drug discovery in oncology are analysed. The ethical implications of using patient data for training AI models, as well as the possibly limited data available for model training, alongside means for preserving patient confidentiality are also discussed. The article concludes that there are numerous promising current and future applications of AI in oncology and mathematical oncology. However, the field as a whole suffers various limitations: some mitigated by the use of AI and some arising from it.

INTRODUCTION

As it stands, there are more than 385,000 cancer cases per year in the UK and the disease is one of the leading causes of death (World Health Organisation, 2024). Cancer is broadly defined as uncontrolled, abnormal proliferation of cells which can invade and alter healthy tissue, resulting in negative physiological effects (O'Dowd et al., 2020). Normal cells can become cancerous as a result of mutations which affect the regulation of cell division as well as the mechanisms that cause cell death, also known as apoptosis. These mechanisms can detect that the cell has mutated and become cancerous, and either rectify this or eliminate the cell. However, when mutated they cannot perform this function. Some of these specific mutations are inherited, but in most cases they occur either sporadically or because of environmental factors such as benzene or asbestos, which damage cells and promote their mutation. As a result, these substances are referred to as carcinogens (Chmielowski and Territo, 2017). Cancerous cells also have the characteristics of blocked differentiation, the ability to spread to other sites in the body (also known as metastasis) and genomic instability, which makes the cell prone to further mutations (Devita et al., 2008). The ability of cancer cells to spread from the initial site of growth to other sites in the body is especially alarming, as this complicates treatment and produces further adverse symptoms if more organ systems are affected.

Existing Interventions

There are several known methods to treat cancer. The first is surgical removal of the tumour, which is mostly suitable in solid tumours which are localised. However, this becomes dangerous if the tumour lies close to vital organs, or if it has spread to other parts of the body (Qazi and Tariq, 2023). Aside from surgery, the most common treatments are chemotherapy and radiotherapy. Chemotherapy involves the use of toxic drugs to target cancerous cells. However, chemotherapy has adverse side effects that cause suffering for patients, involving discomfort and pain over prolonged periods in addition to the damage to the body caused by the toxicity of the drugs(Stevens, 2022). Radiotherapy involves the use of radiation to damage the DNA of cancer cells, thereby impairing their ability to replicate, and as a result the cancerous cells eventually die out without replacing themselves. However, radiation affects the healthy cells of the body, also resulting in adverse side effects (Wong et al., 2017). Targeted therapies and immunotherapies are more recent developments. Targeted therapies target specific molecules which facilitate the growth and spread of cancer, while immunotherapies aim to stimulate the immune system to recognise and destroy cancer cells. These treatments, while promising reduced side effects, are still in their infancy (Qazi and Tariq, 2023).

Due to the nature of these treatments and the negative patient outcomes in cancer, which see only 50% of patients surviving more than 10 years, it is crucial that cancer be detected early to minimise the associated risks (Cancer Research UK, 2015). Similarly, due to these effects and to the vast variety in types of cancer and progression, it is important that treatments be tailored to each patient individually. As a result of this need for individually tailored treatment, the use of tools such as Artificial Intelligence (AI) is becoming increasingly important to improve patient outcomes.

ONCOLOGY AND AI

Oncology is the study of cancer, encompassing prevention, diagnosis, prediction, and treatment. A broad range of techniques such as imaging (for example Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) scans), biopsy (physically extracting and studying cells), blood tests; and even mathematical models are employed to achieve these tasks. These techniques aim to find markers that certain cancers display, for example protein markers and biochemical changes which can be detected using blood tests, but which are sometimes not unique to the cancer and can therefore only be used as a strong indication and not a definitive diagnosis. Imaging can also reveal abnormal masses which indicate cancer. DNA analysis can be used to determine which mutations result in the formation of cancerous cells, as well as individuals who are likely to have inherited such mutations. Long-term studies similarly identify substances which promote the development of cancer and ensure that the public is aware to prevent further instances (Chmielowski and Territo, 2017).

AI is defined as the creation of systems that can perform tasks typically requiring human intelligence such as perceiving and learning, problem-solving, and improving upon itself (Russel and Norvig, 2021). It is not difficult to see how such a system could be useful in many fields, medicine being no exception. Depending on their advancement, AI tools could be used to assist oncologists in every task mentioned above, leading to improved patient outcomes in both the short and long term.

Mathematical Oncology and AI

Mathematical oncology - the study of developing mathematical models to predict the behaviour of cancer and its response to treatments - would integrate well with AI in theory, but this may not be the case in practice. Studies such as Metzcar et al. (2024) find that AI is currently not advanced enough to make a significant contribution in this field. At the time of writing, the use of AI tools in mathematical oncology is limited: deriving novel mathematical equations is not a task that AI has had much success with thus far. This is due to limited access to data, as well as the difficulty of analytically representing relationships in the context of a biological system (Metzcar et al., 2024).

Despite this, AI is still able to find some applications in mathematical oncology, which can only improve as technology develops. An example is the work of Ezhov et al. (2023), wherein an AI spatial model was used to analyse and predict brain tumours in specific patients from magnetic resonance images. This study improved upon its predecessors, which used Partial Differential Equation-based growth-and-response spatial models. A spatial model attempted to predict growth of cancer based on the area around the tumour and the microenvironment of tumour cells (Kuang et al., 2016). Similarly, Benzekry et al. (2020), succeeded in using AI to find survival rates of metastatic cancer in nerve cells. Furthermore, the use of hybrid modelling using Bayesian statistics also seems to be a promising possibility (Metzcar et al., 2024). Such possibilities notwithstanding, it is apparent that the more practical applications of AI, rather than the analytical, are far more advanced. This is due to current limitations in deep learning, which are further hampered by a lack of specific oncological data of the same subject over time. Furthermore, AI use in mathematical oncology poses issues such as unclear indication of errors in initial input which may or may not have carry-over. There is also a lack of a detailed understanding of the relationship between complex input data and the desired output, which is currently simplified due to the aforementioned limitations. These factors play a part in hindering mathematical oncology, alongside the fact that mathematical oncology remains an especially limited field due to the lack of suitable data. This is further exacerbated when it comes to training an AI learning model, which requires extensive data to be accurate (Metzcar et al., 2024).

Use in diagnosis and a case study of the Clinical Histopathology Imaging Evaluation Foundation

The Clinical Histopathology Imaging Evaluation Foundation (CHIEF) is a recent development in the field of clinical AI, devised by Wang et al. (2024). CHIEF is a deep learning system, which modulates the cognition of the human brain in problem solving (Russel and Norvig, 2021). Unlike its predecessors, CHIEF can be used as a general-purpose AI for analysing microscopic slides, requiring little supervision (Wang et al., 2024). CHIEF analyses these microscopic slides for the purpose of evaluating the features of cells, and diagnoses cancer based on appearance of cells and specific features of cancer. CHIEF is multifaceted and has been successful in several endeavours.

CHIEF was trained on more than 60000 whole slide images in order to characterise cancer, which it did successfully (Khened et al., 2021). The training process involves collating training data slides and using deep learning processes to train AI to view the slides and detect both the presence of cancer and its type. This task is currently conducted by pathologists, who also manually view the microscopic slides by looking for the same malignant features that the AI looks for. This can be considered an excellent application of AI, as it can almost completely automate this task.

Some studies have determined that CHIEF is able to carry out this task with greater efficiency than other pre-existing deep learning systems serving the same purpose across a range of different cancers, as shown in Figure 1:

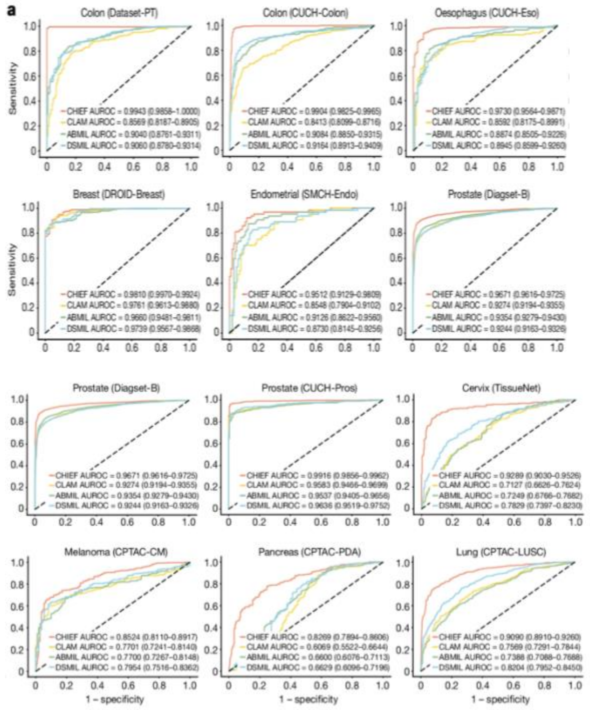

Figure 1: Comparison of Different Deep Learning Models (Wang et al., 2024). Receiver Operating Characteristic (ROC) curves are shown which evaluate the relationship between the sensitivity and specificity of a model, in this case for specific cancers. CHIEF is compared to existing deep learning models. CHIEF model's ROC curve is the orange line in each graph. A larger area under the curve indicates a more accurate model.

Furthermore, the CHIEF framework was also used to systematically predict prevalent genetic mutations across different cancer types which may be involved in the development of that cancer. CHIEF successfully predicted known cancerous mutations in genes such as 'GTF2I' and 'BAP1', indicating that the generalised approach still yields efficacy in this case.

While CHIEF appears to be the latest development in histological AI, there exist numerous uses of AI in the diagnosis of cancer using imaging methods. AI was used by researchers Vachon et al. (2023) to identify invasive breast cancer using low energy X-Ray scans of breasts with relatively high accuracy.

Aiding Prognosis

The use of AI in prognosis remains viable despite the aforementioned limitations. Kinoshita et al. (2023) used an AI prognostic model combined with electronic health records to develop a model to determine the postoperative prognosis of patients based on general measurements as well as organ-specific measurements and analysis. Through accounting for these, the measures of rates of disease-free survival, overall survival, and cancer-specific survival were predicted. The AI was found to be relatively accurate in all measures, with the prediction of cancer-specific survival being of a high degree of accuracy, indicating a very promising application. This is due to the AI analysing a trend based on available real-time data rather than analysing mathematical relationships, thus achieving greater efficiency (Kinoshita et al., 2023).

Prediction of Drug Responses

Another recent development - the PERsonalized single-Cell Expression-based Planning for Treatments in ONcology (PERCEPTION) machine learning model, developed by Sinha et al. (2024) - is built specifically for precision oncology. With this model, treatments are individualised on a patient-by-patient basis, based on specific genetic attributes. The need for an AI model in this endeavour arises because there is a requirement for multiple different treatment combinations due to tumours varying from patient to patient, and even the presence of variations in the same tumour within one patient (Ramón y Cajal et al., 2020).

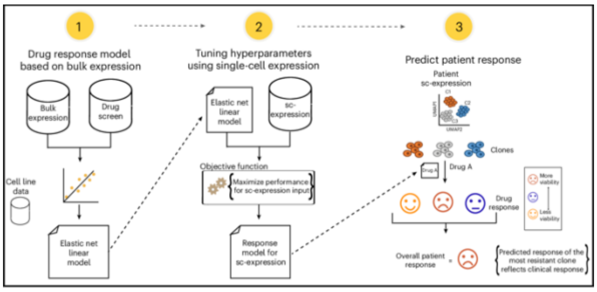

Figure 2: Three Step Process of the PERCEPTION framework (Sinha et al., 2024). Shown are illustrations of the stages involved in modelling within the PERCEPTION framework, numbered 1-3. These are the creation of bulk models, single-cell expression, and prediction of patient response.

PERCEPTION achieves this using a three-step process, as illustrated in Figure 2. Large-scale data demonstrating how different cancers with different specific genetics respond to a drug, based on the genetic attributes and mutations involved, is used to create a prediction model (Dong et al., 2020). This model is used as a basis to create a smaller-scale, single-cell model that predicts which specific genes cause differences in drug responses. Thus, the AI analyses trends in genes and identifies the likely genes which cause differences in drug efficiency and accounts for them in predictions. Finally, the patient response is predicted using a three-step heuristic procedure which is as follows: the genetic data of the patient's tumour is found by analysing the tumour cells, and the major variants among these cells are found. The average genetic attributes of each variant are found and used as an input for PERCEPTION, which then predicts the drug response (Sinha et al., 2024).

The method is comprehensive and, for its development, bulk expression and drug response data from 488 different cancer cell lines were analysed. 133 US FDA-approved oncology drugs were also studied using this model and their performance was computed. Among these, a subset of 44 was further analysed. It was found that the AI used an average of 76 genes as predictive features, having self-identified genes such as 'ABCB1' which controls multi-drug resistance. This shows the efficacy of the model. It was found that PERCEPTION could differentiate drug-resistant from drug-sensitive cell lines with an accuracy of 81%, indicating that the model is relatively accurate in its prediction of drug response (Sinha et al., 2024).

Use in drug discovery

Drug discovery, or the development of new medication for the purposes of treatment, is another endeavour in which AI can be applied. AI can find applications in every stage of the drug discovery process, as illustrated in Figure 3. It can be used to identify target cells or receptors for drugs, and to screen these molecules for attributes such as stability, in order to identify the most suitable options (Urban et al., 2019). Furthermore, AI can be used to adjust small molecules to increase their efficacy, as well as investigate the administration of the drug and other accompanying compounds which aid the drug's function (Kokudeva et al., 2024).

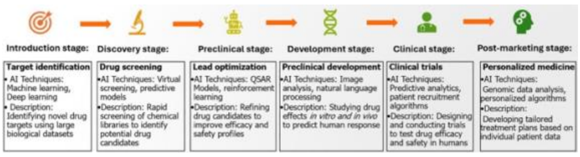

Figure 3: Stages of Drug Discovery and Possible Applications of AI within (Kokudeva et al., 2024). The stages of drug discovery which are introduction, discovery, preclinical, development, clinical, and post marketing are illustrated with reference to applications of AI in each

One good example of the practical application of these principles is an AI machine learning algorithm, eToxPred, which has been used to predict drug toxicity (Pu et al., 2019). Evaluation found that eToxPred was able to predict the toxicity of a compound and whether it will harm organ systems, such as the heart or kidneys, with relatively high efficiency. It helps to screen compounds that may be hard to produce, as well as compounds which resemble existing toxic compounds. It may therefore save significant effort in the process of drug discovery and streamline the process (Pu et al., 2019). This is important as it further reduces elements of trial and error in drug discovery by screening possibilities quickly, increasing efficiency of drug discovery significantly.

Similarly, the Institute of Cancer Research is aiming to develop precision cancer drugs using AI in drug discovery, in collaboration with the Bellvitge Biomedical Research Institute and Vivian Therapeutics (Institute of Cancer Research, 2023). They aim to create drugs targeting the K-RAS protein, as a mutated *KRAS* gene may result in cancer. Currently there are limited drugs which target the K-RAS protein, thus this research facilitated by applications of AI should be a significant advancement in oncology (Jančík et al., 2010).

ETHICS AND LIMITATIONS

Currently, there are various challenges to the development of AI models for the purposes of healthcare. The foremost limitation is the availability of data. Only limited data that is made available for research purposes can be used for training AI learning models. As a result, biases might arise in datasets, thus reducing accuracy (Kolla and Parikh, 2024). The designers of the CHIEF framework (Wang et al., 2024) made a note of this lack of data, and found that a limitation of their study was that they only had a small amount of data about healthy cells available, thus affecting the accuracy of the predictions made by the AI. This is because these learning models are shaped entirely by the datasets they are trained on. This limitation was similarly present in the PERCEPTION model, wherein Sinha et al., 2024, noted that the accuracy of the prediction model was directly dependent on their data, and the predictions would only increase in accuracy as data availability increases.

The field of healthcare is one which relies on transparency and respect of patient autonomy, while tools such as deep learning AI are challenging for humans to interpret. Their decision-making is not always clear, and if these models make mistakes, then the causes must be made known to ensure they are not repeated, as mistakes are often irreversible in the field of healthcare. Furthermore, there is a lack of accountability should a mistake be made by such an AI (Shreve et al., 2022). AI also poses both a threat to patient data confidentiality and a challenge to obtaining informed consent due to lack of AI transparency, as well as the possibility of data leaks which limit the current applications of AI due to a lack of existing legal frameworks (Rigby, 2019).

CONCLUSION

AI used for the purposes of improving patient outcomes in oncology have shown fruitful applications in diagnosis, prognosis, prediction of treatment responses, and drug discovery. However, this paper has argued that current AI networks are not advanced enough to be applied to the highly analytical nature of mathematical oncology. While some applications have been discussed here, several limitations have also been noted. The CHIEF and PERCEPTION frameworks characterise the shift in medical AI from niche applications to something closer to a commercially viable form, while the applications of AI in drug discovery are promising but still undergoing development. The most significant limiting factors to all these developments concern low data availability, noted by nearly all researchers in their respective areas of applications and representing the same limitations faced in mathematical oncology and statistical analysis of cancer for years. However the integration of knowledge-based and data-based networks could yield significant results in the future.

The use of electronic health records presents an interesting solution. However, it is noted that older data does not necessarily contain the advanced parameters now known to accurately train learning models. The crux of the problem lies in how patient data can be recorded on larger scales and without violating autonomy and confidentiality, given the lack of legal guidelines in this matter. The lack of transparency in AI prevents its commercial use, as healthcare is an extremely rigorous field and this would defy the core ethical principles of medicine. These factors currently limit such AI applications to research studies and requires development in both practical and ethical guidelines.

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