Study demonstrates how AI can develop more personalized cancer treatment strategies

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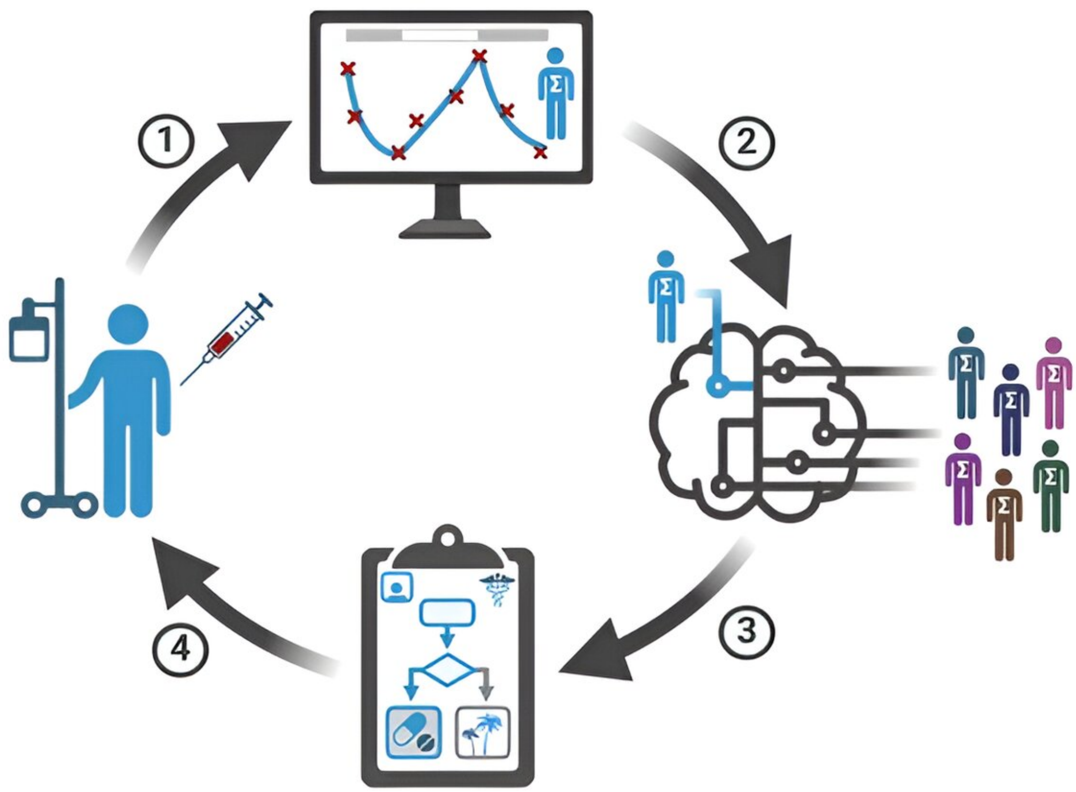

Schematic showing how the AI-informed adaptive therapy would work. Regular patient blood tests (1) enable the size of the tumour to be tracked. A mathematical model is applied to the data to simulate a virtual patient model (2). A generalised deep learning network is fine-tuned on the virtual patient (3), enabling the clinician to extract a practical treatment schedule that is personalised to the individual patient's tumour and treatment history (4) to drive the next round of treatment. Credit: Kit Gallagher, created using Biorender.com

University of Oxford researchers have leveraged the power of artificial intelligence (AI) to develop personalized cancer treatments which could be more effective at preventing patient relapse.

One of the greatest challenges in cancer treatment is maximizing the impact for the patient from drug treatments. Conventional treatment strategies, which focus on killing as many cells as possible, are based on a 'maximum tolerated dose' (MTD) therapy, where the patient continually receives a high drug dose, with no breaks in treatment. However, these frequently fail against metastatic cancers due to the emergence of drug resistance.

Adaptive therapy strategies, which dynamically adjust treatment to suppress the growth of treatment-resistant populations, have emerged as a promising alternative. However, the lack of personalized approaches that account for patient variation limits their efficacy.

In a study, titled "Mathematical Model-Driven Deep Learning Enables Personalized Adaptive Therapy" published in *Cancer Research*, researchers from the University of Oxford and Moffitt Cancer Center in Florida introduce a novel framework that applies deep reinforcement learning, DRL, (a form of AI) to create adaptive therapy schedules for individual prostate cancer patients.

The results indicate that the new adaptive approach could potentially double the time to relapse compared to MTD or non-personalized treatment breaks.

First author Kit Gallagher, a DPhil student at Oxford's Mathematical Institute, trained the DRL network on synthetic data from a mathematical model of prostate cancer, to replicate behavior seen in previous clinical trials. The mathematical model was vital to generate sufficiently large quantities of 'virtual patient' data and allowed the researchers to evaluate treatment schedules that couldn't easily be tested clinically.

The results indicated that the DRL framework consistently outperforms the conventional MTD and adaptive strategies used clinically, delaying relapse for all patients in the test cohort and more than doubling the time until relapse for some patients.

It was also robust to changes or uncertainty in both the patient's treatment response and the time interval between treatments, crucial for the real-world application of this approach.

Importantly, the researchers demonstrated that interpretable treatment strategies could be extracted from the 'black-box' deep learning network, in a form which a clinician would be able to understand and prescribe to their patients.

"Interpretability has long been a significant hurdle to integrating machine learning approaches into clinical practice," said Kit Gallagher.

"When these frameworks are a black box, and we can't understand how they derive treatment recommendations, we can't be confident applying these in the clinic. But our new study shows that this hurdle can be overcome."

The approach can even be used for patients starting new drugs, who do not have a historical record of how they respond to the treatment to inform a personalized schedule. For these cases, the researchers propose a pathway where the patients would initially start a standard treatment cycle.

A 'virtual twin' of this patient would then be created based on their data from this initial treatment, which could be used to fine-tune the DRL model to generate a personalized treatment schedule.

The researchers are planning further studies to refine this method and explore its application to other forms of cancer.

More information: Kit Gallagher et al, Mathematical Model-Driven Deep Learning Enables Personalized Adaptive Therapy, *Cancer Research* (2024). DOI: 10.1158/0008-5472.CAN-23-2040

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