

Artificial intelligence (AI) in medicine: current position and perspectives

The advances, transformations and fears linked to artificial intelligence are raised on a daily basis, and in all areas: safety, work, transport, energy and health. François Le Grand presents his research, performed with Nicolas Houy*, on the applications of AI to medicine, specifically in relation to the optimisation of oncology care protocols. When AI becomes a decision support tool for choosing the most favourable combination of treatments. Explanations.

What is AI?

AI is currently a very fashionable term, which has become almost synonymous with revolution in the medical field. As it is not always easy for external observers, whether they are investors, clients or patients, to know what the technology encompasses, the term can sometimes be misused, particularly in the press releases of certain technologies. For these technologies, the exact role of AI is not always clearly explained and does not even appear to be a relevant solution in every case. The suspicions of observers are therefore legitimate.



Nicolas and I work in this last area.

AI in statistical analysis

AI is an excellent tool for highlighting potentially complex statistical relationships in very large data sets. In medicine, the “simplest” data are medical images, whether photos, X-rays, MRIs, or scans, etc. An image is a piece of static and homogeneous data. In general, medical images are much less complex than a patient’s medical records, for example, which aggregate different types of data (images, blood tests, clinical examinations, physiological data, etc.) and include a time dimension. In addition, these data are available in very large quantities, making it possible to “train” the AI models more effectively. AI is currently being used to make diagnoses based on medical images. The results are excellent and AI is as good as, or even better than, human specialists in the field. On the other hand, AI is highly specialised, and can generally only process one type of image for a disease or family of diseases. Without attempting to be exhaustive, we note the following examples: the use of photos to identify **different types of skin cancer**, x-rays to detect **tuberculosis** or **pneumonias**, and eye fundus images to diagnose **diabetic retinopathy**. In addition to disease detection, x-ray analysis has also been used successfully to predict the **chances of recovery** of cancer patients.

AI results in this area are impressive and make the computer a powerful decision support tool for physicians and radiologists. However, computers are unlikely to replace radiologists any time soon. Other aspects must be kept in mind, namely: human aspects, in particular communicating sometimes upsetting imaging results; legal aspects, linked to liability for a misdiagnosis, which remains possible with AI; and finally deontology, to confirm the AI diagnosis, which may have missed an obvious point that it was not trained for.

AI in optimisation

Nicolas and I work in optimisation, which is another AI application field. We will start by explaining how optimisation can be used in medicine, in particular to establish oncology care protocols. The standard paradigm in chemotherapy is to fight the tumour directly by administering massive doses of cytotoxic drugs over several days, followed by a fairly long rest phase and to then repeat this combined cycle of treatment and rest a number of times. Although this type of protocol works in some cases, it also has the disadvantage of leading to tumour-resistance phenomena, which become increasingly insensitive to treatment. It also has harmful side effects. In addition to attacking cancer cells, cytotoxic drugs also lead to a reduction in the number of blood cells and can thus induce fatigue and immunosuppression. Furthermore, in the standard protocol, the doses administered correspond to the maximum tolerated dose, which is set in such a way that the side effects remain acceptable. In the period 1990-2000, a new

school and associate researcher at ETH Zurich, I am a graduate of École Polytechnique and ENSAE. I also received a doctorate from EHESS while working at Barclays Capital. My primary focus in research has been on risk economics, but for some years now, I also study the applications of artificial intelligence (AI) in health, especially in oncology. My work is published in academic journals such as *Econometrica*, *Management Science*, *the Journal of Economic Theory* or *Plos One*, and I also write tribunes for the French mainstream media (*Le Monde*, *Les Echos*). I have some experience in consulting for non-academic partners as well.

More information on François Le Grand:

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the opposite of the standard paradigm. Clinical trials have not provided a clear conclusion between the two paradigms, suggesting that other types of protocols should be explored. Nevertheless, using clinical trials to test protocols is long, expensive and risky because a clinical trial is expensive and the number of possible combinations is very high. Fortunately, in recent years, modelling and simulation tools have been developed that enable new protocols to be tested *in silico*. Some of these protocols have been the subject of promising **clinical trials**. Numerical simulations can be used to find the most effective protocol (doses and injection planning) in the fight against tumours, provided that the level of toxicity – and therefore side effects – is tolerable for the patient.

Nevertheless, optimising all protocol dimensions – doses, injection planning – is a difficult exercise, even with *in silico* simulations. Over a fairly standard treatment period of 300 days, there are approximately 10^{90} possible combinations, even if we limit ourselves to only two alternatives per day, namely injection of a given dose or the absence of injections. To put this into perspective, this is 10 billion times the number of atoms in the universe, which is estimated at 10^{80} . Given that simulating a combination of treatments can take more than one minute of computation time, we can easily see that optimisation with standard methods (such as dynamic programming) is not a viable solution. The typical methods for making optimisation feasible are to simplify the underlying medical model and to impose additional limitations on the desired protocol. A classic simplification is to require the protocol to correspond to a cycle of given duration that is repeated identically a certain number of times. Nicolas and I propose a third way for optimisation, which involves using artificial intelligence algorithms. The algorithms we use belong to the Monte-Carlo Tree Search family, which has been popularised by DeepMind's victories over Go champions. We perform an approximate optimisation, because effective optimisation is not possible. Our method is therefore closer to heuristic optimisation; however the results we obtain confirm the usefulness of our approach.

What are the advantages of our solution? There are numerous advantages. First, there is no need to simplify the underlying medical model or impose optimisation constraints (relating to the cycle, for example). The entire problem can be optimised in all its complexity. In addition, this solution is very flexible and easily adapts to new underlying medical models, complex objectives, or multiple toxicity constraints (often measured by several factors simultaneously), etc. We highlight two possible applications that we have developed. The first is to couple this optimisation technique to a learning algorithm, meaning that the protocol can be adapted to each patient according to their reactions to the treatment. In other words, this solution opens the door to personalised care protocols. In addition, it is important to note that this personalisation is dynamic in the sense that the patient's protocol is adapted in real time, depending on the patient's condition and

biomarkers). This personalisation is static as it is performed “once and for all” at the beginning of the protocol. AI algorithms, on the other hand, offer the possibility of dynamic personalisation, which adapts in real time to what is learned from the interaction between the treatment and the patient. Our second application concerns the combination of treatments, or combination therapy. Our algorithm is able to take into account not only chemotherapy but also immunotherapy and combination therapy. Combination therapy may include multiple lines of chemotherapy as well as a combination of chemotherapy and immunotherapy or even the use of products to manage the toxic effects of chemotherapy (e.g. a granulocyte colony-stimulating factor to combat neutropenia). This application, in addition to optimising combination therapy, also makes it possible to compare the care effectiveness of different treatment lines and thus to choose the line with the most favourable prognosis. Standard care protocols today consist of combinations of chemo- and immunotherapy and several combinations are generally available for each type of cancer. Our solution offers decision support to assist in the choice between these different combinations.

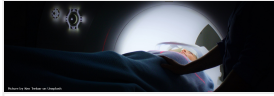
Other applications in the pipeline

For all these applications, the results of the *in silico* simulations are unanimous. They show that, compared to standard protocols, optimisation via AI offers significant efficiency gains for a comparable level of toxicity. Other applications are obviously possible and we have also worked on the question of administering EPO in cases of anaemia, again using *in silico* simulations. We are currently beginning to explore ways to determine the extent to which our *in-silico* results can be transposed *in vivo*.

**This article, previously published on [LinkedIn](#) on 21 September 2018, was co-authored with Nicolas Houy, a researcher at the CNRS and at the Groupe d'analyse et de théorie économique (GATE) at Lyon Saint-Étienne.*

Further readings...

- Houy N., Le Grand F. (2018). Optimal dynamic regimens with artificial intelligence : The case of temozolomide. ***PLOS ONE***, 13 (6).
DOI: 10.1371/journal.pone.0199076.
[Read article online](#)
- Houy N., Le Grand F. (2018). Administration of temozolomide: Comparison of conventional and metronomic chemotherapy regimens. ***Journal of Theoretical Biology***, 446: 71-78.
DOI: 10.1016/j.jtbi.2018.02.034.
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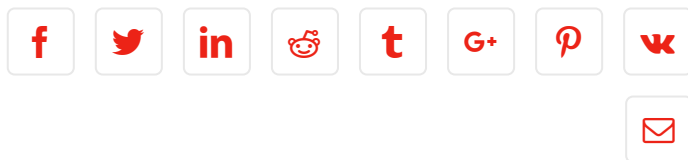
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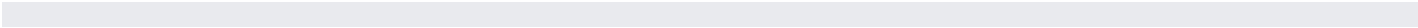
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