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Editorial

Arti ıcial intelligence in Oncology: Doctor in silico?

Uso da inteligência artificial em Oncologia: Doctor in silico?

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The definition of a diagnosis and the respective treatment is based on the use of data collected from the patient, which, contextualized in previous experiences, allows us to associate the observed pattern (signs, symptoms, ancillary exams) with some known patterns. Thus, the (already enormous) growing volume of information available from molecular analyses, increased quality and safety of imaging exams, and progressive discoveries about the health-disease process helps physicians define more precisely the best course of action in each case. Despite these advances, data processing and patient assessment still depend on human beings: fatigable, error-prone, costly, and time-consuming training.

In recent decades, mathematics and statistics have been explored to aid clinical decision making and better organization of knowledge. One area that has received attention is artificial intelligence (AI). This is a term that encompasses different algorithms capable of "learning" (or being "trained") to perform classification or regression tasks from prior information without explicit programming. Examples of such methods include decision trees, linear regression, Bayesian networks, and neural networks. Although extremely complex, these modalities comprise simple operations that could generally be done by humans, but which, by their sheer quantity, would take years to do analogically, but seconds to days (in extreme cases) for machines.

Hence, the applications of this technology in Medicine have been studied. In image analysis, for example, the assessment of pre-defined characteristics (shape, intensity, and tone homogeneity of the region of interest, and mathematical transformations of these values), and/or the employ of neural networks and computer vision techniques, are workable through AI. With these methods, it is possible to find correlations not previously identified by humans.

In digital pathology, slides are digitized with high definition, one pixel of the image corresponding to approximately 0.25 micrometer, and each slide having around 15 gigabytes of information[1]. The evaluation of different tissue features, from cell shape to color patterns in nuclei and other cell structures, can aid in the identification of, for example, stromal and epithelial tissue, clusters of normal or tumor cells, and even

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stromal or tumor-infiltrating lymphocytes. This type of analysis is called Pathomics. This technology was used by Wang et al.[2] to detect a subgroup at higher risk of recurrence in patients with stage I-II non-small cell lung cancer (NSCLC), suggesting a benefit in disease-free survival and overall survival with adjuvant chemotherapy in this population.

A similar strategy is also employed in Radiology. In an image exam file, called DICOM, each pixel can have from 12 to 16 bits, i.e., it can assume from 4,096 to 65,536 shades of gray. The monitors used for reading image scans can process up to 8 bits per pixel, or 256 shades of gray[3]. Therefore, only 0.39 to 6.25% of the available information reaches the eyes of the Radiologist. This percentage can be increased by assessing all the raw data in the file, i.e., Radiomics. Wang et al.[4] for example, by combining image evaluation using neural networks, extraction of pre-planned tumor features, and clinical features, was able to predict *EGFR* (Epidermal Growth Factor Receptor) gene mutation status and PD-L1 immunoexpression patterns in NSCLC from chest CT scans with reasonable accuracy (0.62-0.84). Oncologists routinely use these variables to define treatment indications for patients with NSCLC.

Besides image recognition, AI has also been used for text reading and information extraction as Natural Language Processing (NLP). This modality can help researchers read free-form text in medical records and transform it into tabular data. Through NLP, it was possible to analyze thousands of medical records and compose risk classifications for recurrent deep vein thrombosis and bleeding in patients on anticoagulation with real-world data[5,6].

In addition, in the field of molecular analyses, diagnostic technology using an algorithm used to identify defects in homologous DNA recombination from single nucleotide polymorphisms (SNPs) has been approved for clinical use to select those patients who are candidates for PARP (poly ADP-ribose polymerase) inhibitors as maintenance treatment in ovarian cancer[7].

Despite providing interesting and potentially useful concepts, for their implementation in clinical practice, these models must go through several steps, namely: preparation and data collection, creation of the initial model, external validation, creation of the platform for use, evaluation of the impact on decision-making, and implementation[8]. Most currently published models are still in the validation phase. However, this does not prevent the lay media - and often the specialized media - from reporting the results as a true machine revolution, while we are still discovering the potentials and limitations of these approaches, and the expectations placed on them may not match the results[9,10].

Thus, when reading a publication on AI models, one should understand some of the biases that may be present in the study. The production of a reliable model depends on the input of large numbers of patients and their characteristics. Select groups of these variables can create a predictive value for the desired outcome, and this process revolves around quality data generation and adequate computational power. As for the external applicability of the developed model, it may be impaired by initially unforeseen variables: e.g., variations in the preparation of histological sections or the execution of radiological exams generate analysis biases, i.e., erroneous results resulting from substandard data, known as “garbage in - garbage out”. Data separation problems can also generate spurious correlations, which would hinder generalization for some populations. Finally, when producing a result, it is often not possible to understand completely what was analyzed by the algorithm, generating a `black box` effect, and uncertainty in interpreting the data obtained. These difficulties, when added together, have generated great discussions in the field of AI in Medicine, such as the possible biases in to determine ethnicity and gender of patients through imaging exams, and the difference in performance of algorithms according to these variables[11,12]. To better address some of these biases, guidelines and quality criteria have been established[8].

In conclusion, despite the great potential of AI to uncover patterns unidentifiable to the human eye, we are still far from creating commercial-quality complex and safe models. Greater understanding of these techniques and their limitations will enable the creation of algorithms with the ability to amplify the accuracy and productivity of future physicians.

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