Artificial Intelligence in Radiotherapy

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Summary

Back in 1999, Bill Gates wrote about advances expected to take place in the healthcare of the future in his book "Business at the speed of thought". He described the complete flow of information in a pathway surrounding a patient picked up by the ambulance to the moment of discharge from the hospital, including presentation of patient's status in the ambulance, signing off of the documents on the go, analysis of the best treatment options by the doctors based on the digital documents prior to patient's arrival to the hospital, digital decision making, treatment prescription and delivery, and even payment. The whole process was presented as an operational improvement that will help medical systems become smarter with patients. This may not be the first time the idea of information technologies has been used in the context of medicine but it has most definitely sealed the direction in which modern medicine was inclined to go.
Radiation therapy is a branch of medicine that has been heavily dependent on information technologies since 1970s and 1980s, which are considered as the age when orthovoltage era has ended and the new innovative era began. The next milestone in development happened in 1990s when the use of sophisticated computer technology allowed for the development of 3D conformal radiotherapy and later other types of more complex treatment options. Use of computers has not only helped develop treatment options but has also found its use in the radiotherapy process.

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Introduction

In order to deep dive into the subject, we need to adopt some of the widely used definitions:

Artificial Intelligence (AI) and Machine Learning (ML). AI is defined as the potential for a machine to perform the task that would require human intelligence [1], while machine learning is the implementation of the compute methods that support AI. [2].

Deep Learning (DL). A subset of ML allowing computational models composed of multiple processing layers to represent data with multiple levels of abstraction through backpropagation algorithm [3]. Basically, DL could be defined as the process of learning data that are not provided by human operators but are derived by use of statistical calculation algorithms.

Deep Neural Networks (DNN). DNN are a family of learning algorithms in which networks of simple units are interconnected to perform a more extensive computation, and where learning involves simultaneously training the parameters of all units in the network [4]. Figure 1 depicts the above-mentioned scenario.

The radiotherapy process consists of 5 steps: patient positioning and immobilization, simulation, treatment planning (TP), patient-specific quality assurance (PSQA) and treatment delivery. Each is either IT dependant or greatly impacted by IT.

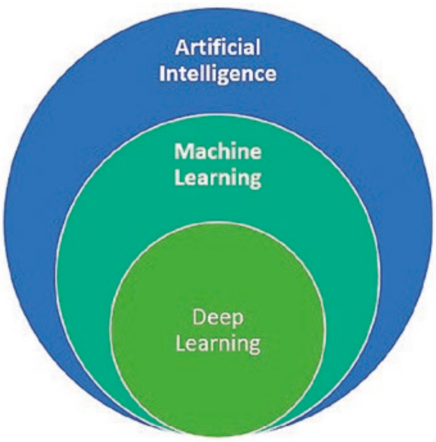

Figure 1. Artificial intelligence, machine learning, and deep learning; Source: Nadia Berchane (M2 IESCI, 2018)

Segmentation of target and organs at risk

Main approach to test AI for target and organ at risk segmentation is based on the training of an ML system followed by the assessment of its performance compared to a gold standard (e.g., manually delineated expert cases) by means of a known metrics of overlapping comparison (Figure 2). Several authors applied AI to target volume definition in different anatomical sites: head and neck cancer [6], prostate cancer [7][8], lung cancer [9], rectal cancer [10], brain metastases [11], and breast cancer [12]. Fifty-two patients affected by oropharyngeal cancer were used at the MD Anderson Cancer Center on the subject of developing a deep learning algorithm able to identify physician contouring pattern and voxels forming high-risk target volume. Authors concluded that predicted contours could have been clinically implemented with only minor changes [13]. McCarroll et al. study showed that half of the autocontours obtained were not edited for use in planning, while contours of normal structures generated by autocontours algorithm were deemed acceptable for clinical use [14].

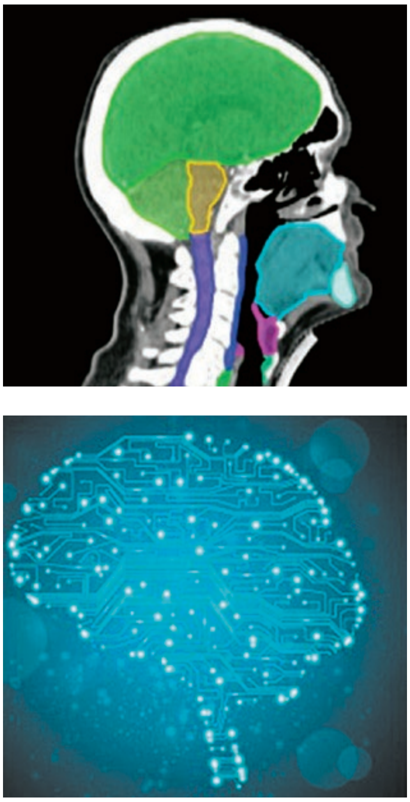

Figure 2. Autocontours generated by Mirada's Deep Learning Contouring, "neural networks" image

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Treatment planning

TP may be the most computer dependant step in the radiation therapy chain and one part of it is already based on the AI as it consists of dose calculation which is solely done by means of computer technology and Monte Carlo (MC) simulations. Radiotherapy treatment planning is a laborious process, sometimes taking hours or even days to complete. Plan improvements often require many iterations: physicians may need to interact with human planners back and forth what leads to tremendous human efforts and time consumption. ATP (automated treatment planning – Figure 3), on the other hand, has successfully reduced plan generation time and repetitive human interactions allowing human planners to devote more time to explore the optimal dosimetry for individually optimized treatment planning [15, 16].

Revision of the past cases is the practice used to improve manual treatment planning efficiency and quality. The approach known as the knowledge-based planning (KBP) is used wherein statistical models are developed with the aim to pinpoint important elements from the prior good cases. This approach is particularly helpful in reducing repetitive activities that consume time in the process of making a treatment plan. In dose-volume histogram (DVH) based inverse optimization, DVH constraints have a crucial role in the process of producing good quality plans. If they are consistent, the algorithm will quickly find an optimal solution with a well-balanced dosimetric outcome.

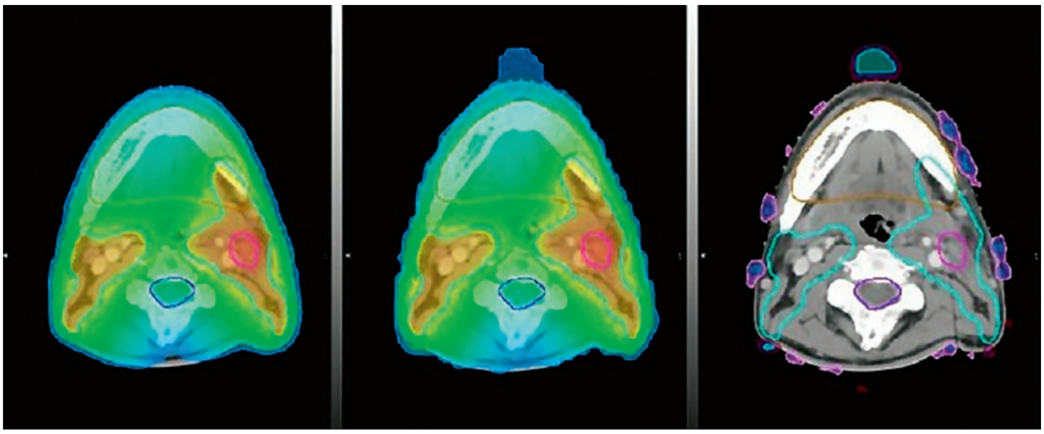

Figure 3. Dose distributions for a head-and-neck cancer patient. Left : predicted plan; centre: automatically generated plan; right: voxel-by-voxel difference maps. (Courtesy: Med. Phys. 10.1002/mp.13271)

DVH-based knowledge modelling has therefore been the source for many new studies. Those automated systems use predicted DVH curves that can be further used in two ways by planner as an input for dosimetric constrains for manual optimization or as an input for automatic treatment planning system.

Yuan et al. research study presented models for prostate and head and neck intensity-modulated radiation therapy treatments saying "The geometry of an organ at risk (OAR) relative to the planning target volume (PTV) was represented by the distance-to-target histogram (DTH), and characteristic geometry and dosimetric features were derived from DTH and DVH by principal component analysis (PCA), respectively". This approach gives a precise dose prediction in both modeled sites [17]. However, due to lack of special information, DVH-based approach is still not a perfect solution as the planners might need additional time to handle certain cases with complicated OAR/target geometry [18].

An additional limitation to successful AI-based ATP implementation is a requirement for a large patient base that can be primarily achieved through large multicentric trials based on rigid trial inclusion criteria. Still, even though the future of AI in ATP remains in motion, radiotherapy treatment planning is not likely to become "human-less" in the next coming years as requirement for control and oversight of treatment planning process in the clinical treatment planning workflow will remain.

Treatment delivery

Modern radiotherapy requires high precision standards and methods to predict deviations from expected dose distribution occurring during treatment dliverty and that may increase certainty about delivery and improve overall quality of treatment. In simple terms, AI could be used to extrapolate a prediction of dose truly delivered to the patient. Tumor and anatomical changes that occur during the course of radiotherapy treatment can dramatically affect the planned isodose distribution and alter the outcome of overall treatment. Another important source of deviation is discrepancy between planned and delivered movements of multi-leaf collimators. An ML approach has been developed to predict these discrepancies from the plan files (i.e. leaf position and velocity, movement toward or away from the isocenter of MLC etc.). Results showed that predicted leaf position was significantly closer than planned if compared to delivered position, yielding a more realistic representation of plan delivery, and reflected in a closer agreement in terms of dose volumetric parameters in comparison to delivered dose [19]. Another issue that could be solved by use of AI is the need for accurate pretreatment quality assurance procedure. A DNN was tested in this area by Mahdavi et al. using Electronic Portal Imaging Device fluence maps of the anteroposterior prostate and nasopharynx RT fields as an input, evaluating dose map as output. Results showed excellent agreement between output and dose maps predicted by the treatment planning system [20]. The next big step achieved by introduction of AI in treatment delivery was automatization of adaptive radiotherapy.

Adaptive therapy involves the ability to alter a radiotherapy treatment plan based on tumour and anatomical changes over a course of therapy. The goal is to better target the tumour based on daily anatomical changes, reduce dose to healthy tissue and potentially improve overall outcomes. Without AI, achieving this has typically required time-consuming re-planning between treatment sessions or monopolizing a linac for an extended period while a patient waits on the treatment couch for new plans to be generated. Neither of these alternatives has been deemed practical or affordable at scale, as very often clinics do not have the resources even if they have the tools. In the years to come many challenges will remain to be tackled for the successful delivery of adaptive radiotherapy.

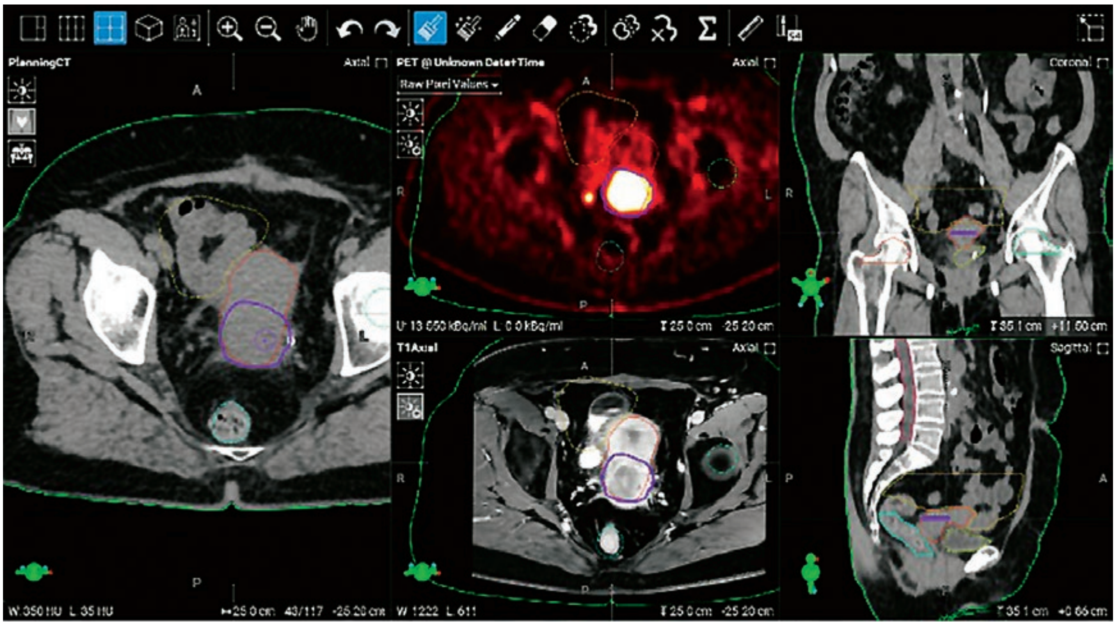

Figure 4. Assisted contour generation; Varian Medical Systems, Palo Alto USA. Combining multimodality imaging

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Conclusion

Even though these approaches will most definitely bring impressive speed and accuracy to the radiotherapy process, all researchers agree that the transition is not expected to be easy. Bridge and Bridge list three areas that will suffer the greatest damage: creativity, innovation, and patient safety (Pete Bridge, 2019). They additionally stress the importance of considering moral and ethical issues in using AI as well as the potentials of lack of empathy and intuition that place a patient to a position of being a mere “diagnosis” instead of a person who requires a holistic treatment approach. Additional problems identified also include system unreliability and making mistakes that a human would not make, as well as maintaining such a complex system what inevitably raises an issue of increased costs. Still, it is expected that the AI will in the future be more implemented in the radiotherapy workflow and take many responsibilities away from the clinical team. ■

Sažetak

Još 1999.g., Bill Gates je u svojoj knjizi “Poslovanje brzinom misli” pisao o napretku koji se očekuje u zdravstvu budućnosti. Opisao je cjelovit protok informacija vezano uz pacijenta kojeg je preuzeo zdravstveni tim hitne pomoći, od ambulante pa sve do otpusta iz bolnice, uključujući prikaz stanja pacijenta, potpisivanje potrebne dokumentacije, analizu mogućeg liječenja na temelju digitalnih nalaza prije dolaska u bolnicu, digitalnog odlučivanja, odabir lijekova i procesa liječenja, pa čak i plaćanje.

Radioterapija je grana medicine koja je u velikoj mjeri ovisna o informacijskim tehnologijama, od 1970.-ih i 1980.-ih, koje se smatraju dobom kada je završilo ortovoltažno doba i započelo novo inovativno doba. Sljedeća prekretnica u razvoju radioterapije dogodila se 1990.-ih kada je upotreba sofisticirane računalne tehnologije omogućila razvoj trodimenzionale konformalne radioterapije i ostalih složenijih mogućnosti terapije ionizirajućim zračenjem. Računala nisu samo pomogla u razvoju, nego su postala neizostavnim dijelom radioterapijskog procesa.

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