The Emergence of Artificial Intelligence within Radiation Oncology Treatment Planning

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Abstract

Background: The future of artificial intelligence (AI) heralds unprecedented change for the field of radiation oncology. Commercial vendors and academic institutions have created AI tools for radiation oncology, but such tools have not yet been widely adopted into clinical practice. In addition, numerous discussions have prompted careful thoughts about AI's impact upon the future landscape of radiation oncology: How can we preserve innovation, creativity, and patient safety? When will AI-based tools be widely adopted into the clinic? Will the need for clinical staff be reduced? How will these devices and tools be developed and regulated? **Summary:** In this work, we examine how deep learning, a rapidly emerging subset of AI, fits into the broader historical context of advancements made in radiation oncology and medical physics. In addition, we examine a representative set of deep learning-based tools that are being made available for use in

external beam radiotherapy treatment planning and how these deep learning-based tools and other AI-based tools will impact members of the radiation treatment planning team. **Key Messages:** Compared to past transformative innovations explored in this article, such as the Monte Carlo method or intensity-modulated radiotherapy, the development and adoption of deep learning-based tools is occurring at faster rates and promises to transform practices of the radiation treatment planning team. However, accessibility to these tools will be determined by each clinic's access to the internet, web-based solutions, or high-performance computing hardware. As seen by the trends exhibited by many technologies, high dependence on new technology can result in harm should the product fail in an unexpected manner, be misused by the operator, or if the mitigation to an expected failure is not adequate. Thus, the need for developers and researchers to rigorously validate deep learning-based tools, for users to understand how to operate tools appropriately, and for professional bodies to develop guidelines for their use and maintenance is essential. Given that members of the radiation treatment planning team perform many tasks that are automatable, the use of deep learning-

based tools, in combination with other automated treatment planning tools, may refocus tasks performed by the treatment planning team and may potentially reduce resource-related burdens for clinics with limited resources.

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Introduction

Advancements in the treatment of cancer arise from a plethora of sources, ranging from basic laboratory science to data science. This is especially true of radiation oncology, a field which delivers ionizing radiation with multi-modality therapies (e.g., photon, electron, proton), probes patient anatomy with multi-modality technologies (e.g., CT, MRI, US), and manages vast quantities of multi-modality data (e.g., longitudinal, demographic). Such data informs a highly diverse and highly trained team of health-care professionals to make decisions so that a patient's radiotherapy treatment is tailored to their needs.

Recently, advancements in artificial intelligence (AI) have emerged; their application to the field of radiation oncology has been demonstrated by many authors [1–19]. While commercial vendors and academic institutions have created AI tools for radiation oncology, such tools have not yet been widely adopted by clinicians into clinical practice. In addition, numerous discussions have prompted careful thought about AI's impact upon the future landscape of radiation oncology: How can we preserve innovation, creativity, and patient safety? When will AI-based tools be widely adopted into the clinic? Will the need for clinical staff be reduced? How will these devices and tools be developed and regulated?

Many have stated that the future of AI heralds unprecedented change for our field, but what of the past technological innovations that have been instrumental in establishing the field of radiation oncology as it is today? In this work, we examine how deep learning (DL), a rapidly emerging subset of AI, fits into the broader historical context of advancements made in radiation oncology and medical physics. In addition, we examine a representative set of DL-based tools that are being made available for use in external beam radiotherapy treatment planning and how these DL-based tools will impact members of the radiation treatment planning team.

AI tools referred to in the work are those which can perform intelligent tasks. ML (machine learning) tools are a subset of AI tools which automatically improve through experience and reliance upon data. Finally, DL tools in this work are ML tools which use artificial neural

networks that mimic the structure of the brain and can learn without explicitly being programmed. Further description of AI can be found in the work by Boldrini et al. [15].

Past Transformative Innovations

Many economic forecasts predict how AI will impact healthcare and the global economy in the coming years. For instance, AI in the healthcare market is expected to grow from approximately 2 billion USD in 2018 to 36.1 billion USD in 2025 [20]. Another analysis by PriceWaterhouseCoopers predicts that AI-based productivity gains alone will add 6.6 trillion USD to the global economy in 2030 [21]. Such projections predict positive economic impact for the near future, but how are we to know if they are accurate or just hype? The Gartner hype curve, introduced in 1995, illustrates the progression of emerging technology from conception to adoption and has since helped to inform market and technology trends [22]. For each emerging technology, expectations from a target audience (e.g., the field of radiation oncology) about the technology is plotted as a function of time and exhibits a characteristic, pulse-like behavior. Progression from one phase to another is a function of many variables and may not necessarily be experienced by each technology. Although hype curves are designed to help inform companies when they should invest in a technology, we re-designed this event-based hype curve to be informative of technology trends within radiation oncology. From a technological standpoint, two past technological innovations have shaped the field of radiation oncology; these are Monte Carlo simulations (MC) and intensity-modulated radiotherapy (IMRT). Along with DL-based segmentation, these innovations are featured below in Figure 1 to provide context for how past transformative innovations have developed over time to become clinically adopted. Although other innovations (e.g., image-guided radiotherapy, electronic medical record) significantly disrupted and shaped current clinical practice, only the abovementioned innovations were chosen to be included in this work.

Events in the “innovation trigger” (yellow) phase are seminal works that are products of inventions, research and development, and laboratory prototypes that trigger further innovation. Publications from the literature in the form of scientific works, review articles, and industrial white papers are some examples of information sources that have increased the expectations of each technology.

Fig. 1. Hype cycle. This figure features a hype cycle curve for three major innovations in radiation oncology (triangle: Monte Carlo; square: Inverse optimization/IMRT; circle: deep learning-based contouring). The curve depicts expectations by the target audience (those in radiation oncology and medical physics) as a function of time. Yellow, magenta, cyan, green, and blue portions of the curve denote “innovation trigger,” “peak of inflated expectations,” “trough of disillusionment,” “slope of enlightenment,” and “productivity plateau” regions, respectively.

During the “peak of inflated expectations” (magenta), first generation products and positive media coverage yield the highest expectations at this point in the curve. The “trough of disillusionment” (cyan) is a time when failures, negative press from the media, and consolidation of the product occur before second and third generation products restore target audience confidence – noted by the green portion of the curve as the “slope of enlightenment.” The final high-growth phase, noted by approximately 20% target audience adoption, is the final portion of the curve (“blue”), and is called the “productivity plateau.” In this work, we have selected various events considered to be significant to each technology. Such events

are meant to inform the reader of prominent phases in each technology’s development, but are by no means exhaustive.

Monte Carlo Method

Regarding Monte Carlo method’s “innovation trigger,” Ulam and Von Nuemann were credited for creation of the Monte Carlo method in 1947 after Ulam was inspired by a thought experiment over solitaire and shared it with his colleague, Von Neumann. Another was a seminal book chapter by Berger in 1963 on electron transport, which formed the basis of early code for electron transport [23]. Rogers, in his thorough review of MC, noted

that from 1967 to 2000 Monte Carlo paper citations doubled every year in PMB or MedPhys [24]. In the “peak” region, MC methods were being developed for the formulation of dose point spread kernels and the field experienced significant acceleration. Although we note no events in the “trough” portion of the curve for MC, computational challenges stemming from hardware limitations slowed adoption. Later, widespread adoption of MC was evident in recommendations stemming from American Association of Physicists in Medicine (AAPM) Task Group 51’s MC-based reference dosimetry factors [25], authors noting the departure from approximation based dose calculations to those using MC [24], and implementation of MC methods in commercial treatment planning and commissioning [26, 27].

Inverse Optimization/IMRT

For IMRT and inverse optimization, Brahme’s group was responsible for work related to solving the “inverse” problem, first commercial development of MLCs, and algebraic inverse planning. Many other important events in the history of IMRT are noted in reviews by Bortfield [28] and Cho [29]. Carol [30] treated the first patient with IMRT in 1994, marking the “peak” portion of the curve. Although IMRT was revolutionizing the field of radiotherapy, the first catastrophic failures occurred in the 1990s and early 2000s [31], resulting in patient injury, death, and subsequent calls from governing bodies to improve how IMRT was commissioned and managed [32]. For “slope of enlightenment” and “productivity plateau” portions of the graph, evidence of growing clinical adoption for IMRT was noted by various studies [33, 34] and AAPM task group reports [35]. Although not discussed in this work, many other significant innovation triggers and key innovations in IMRT were soon to follow such as volumetric-modulated arc therapy [36] and release of Varian’s RapidPlan (obtaining 510(k) clearance in 2013).

Deep Learning

Although the idea of AI was conceived decades before, Long et al. [37] and Ronneberger et al. [38] introduced encoder-decoder models (FCN and UNET) in 2014 and 2015 to the computer vision community, enabling powerful pixel-wise classification models to be made using convolutional-neural-networks. These developments in semantic segmentation served as catalysts to drive advancements in medical image segmentation and DL in the “innovation trigger” portion of Figure 1. When surveying the literature for “deep learning” and “artificial intelligence” articles, Shen et al. [13] noted exponential growth

in publications for relevant medical physics journals since 2015. The first company to release a DL-based contouring tool and gain US FDA (510k) clearance was Mirada’s DL-CExpert [39] in 2018 and is denoted as a “peak” event in Figure 1. As of July 2019, Gartner noted that for AI-based developments in industry, deep and ML were on the edge of exiting the “peak” phase [40]. As noted in this report, DL technologies are projected to be adopted by industry (enter the “plateau of productivity”) within the next 2–5 years [40]. These developments in DL have resulted from gains made in GPU-processing. As Jia et al. [41] predicted in their article on GPU-based high-performance computing for radiation therapy, these have enabled paradigm-shifting technologies to emerge in the clinic.

The Path to Clinical Adoption

Upon further inspection of Figure 1, the MC and IMRT time interval from “peak” to “plateau” was approximately 20 and 10 years, respectively. This can be deduced by subtracting the times between events in the “plateau” and “peak” phases for MC and IMRT. Based on forecasts and predictions mentioned above, the time from DL’s “peak” to projected “plateau” is less than 5 years. This observation may indicate that the time from conception to adoption for software-based advancements in radiation oncology is occurring at faster rates than for past software-based advancements. The transformative technologies we have selected in this work (MC and IMRT) are computationally intensive tasks, which are clinically relevant to radiotherapy, but can have limited clinical viability when computation times are too large. This is especially true for adaptive therapy, image-guidance, and other time-sensitive procedures requiring computational resources. However, with more computing power available than ever before, technologies that previously were limited by computing power now offer friendlier interfaces, are more programmable, and are more portable. Such examples include TPS workstations with onboard GPUs, clinical servers managed by high-performance computing centers, and web-based platforms that provide access to high powered computing resources. For these reasons, the uptake of DL-based tools may not be hindered by computational limitations as Monte Carlo and IMRT once were, but rather by accessibility of the resources to run such tools. Thus, further advances of DL will be driven by availability of high-quality data, especially since the majority of models in development by industry and academia rely on supervised learning approaches for tools made for radiotherapy treatment planning. As more DL tools become commercially available,

their integration into clinical practice may largely depend on accessibility to DL-resources, with the internet being the most direct approach to web-based, DL-based tools for facilities that cannot obtain computing clusters or machines with onboard GPUs.

Avoiding the Trough, Increasing Safety, Preventing Harm

As noted above, and by other technologies tracked in previous Gartner reports, timelines for adoption can be predicted. However, the events (e.g., device malfunction, operator failures) causing patient injury and death often cannot be predicted, like those seen from IMRT in the “trough” portion of the curve. According to AAPM Task Group 275: Strategies for Effective Physics Plan and Chart Review in Radiation Therapy, three of the top ten high-risk and high-severity failures in treatment planning are from “wrong” or inaccurate MD contours, improper margins for the planning target volume, and “wrong” or inaccurate dosimetrist contours [42]. An important question to consider is: can DL-based treatment planning tools reduce such failures through automated second checks? While TG 275 notes that automation cannot entirely replace human decision making, it can “improve efficiency and effectiveness and allow physicists to focus more attention on the review tasks that require human judgment” [42]. In addition, automated tools can introduce standardization, a key component of error prevention [42], into many aspects of treatment planning. Many of the DL- and ML-based tools currently in development for automated treatment planning are discussed in a review by Wang et al. [19]. Although most tools discussed in this review have not been explicitly been developed for quality assurance purposes, many could be harnessed as independent verification tools for existing clinical processes. A few DL-based tools have been developed for QA/QC and employ a fully automated, dual expert approach for cervix, chest wall, and head and neck [43–45]. This dual expert approach performs treatment planning tasks (e.g., contouring, isocenter detection, field aperture creation) using independent models, and flags erroneous contours or plans based on metrics which quantify agreement between the two methods. Such an approach has been found to be effective in increasing the detectability of treatment planning failures when assessed by FMEA for cervix and ROC analysis for the head and neck [45, 46].

Like all AI-based treatment planning tools, DL-based tools must be safely and properly implemented so as to not introduce errors from new failure modes, poor hu-

man factors engineering, automation bias, or improper use [11, 42, 47]. Prior to commercial distribution of the tool, proper regulatory guidelines (e.g., FDA, CE mark) may need to be satisfied. For manufacturers seeking to gain US FDA clearance, manufacturers must complete the approval process and adhere to policies regulating uses of software as a medical device (SaMD) [48]. This ensures that SaMD reaching patients and healthcare operators is safe and effective. For AI-based tools to keep pace with medical and technological advancement, constant modification of the AI-based SaMD (e.g., continuous learning) may be required. However, because such changes may impact the safety and/or clinical functionality of the SaMD, many approved AI SaMD have been solutions with “locked” algorithms (not allowing iterative improvement). While this is meant to safeguard patients and the healthcare industry, the initial framework regulating SaMD was not designed with adaptive algorithms in mind. Discussions involving a safe regulatory framework that address the evolving and adaptive nature of AI SaMD are currently underway [49]. Implementation of these tools will also require department-wide efforts coordinated with radiation oncologists, dosimetrists, and physicists to implement quality control and quality assurance programs.

Such tools could be benchmarked or maintained through the creation of institution or guideline-specific datasets (image sets with high-quality clinical contours). For DL-based tools, periodic performance upon datasets could be used for initial validation and QA/QC programs, similar in principle to recommendations by Brock et al. [50] in AAPM TG 132 for image and registration and fusion algorithms. Within the next 2–5 years, the projected adoption of DL-based tools may also be accompanied by studies elucidating the impact of automatic QA on treatment planning failure incidence rates.

Impact of Emerging Technology

Accessibility and Deep-Learning Based Tools

As noted by both academic and industry experts, DL-based contouring has been shown to be comparable or preferable (via efficiency/time advantage) over manually drawn contours for normal tissue structures [51–53], and has also achieved accuracy that is comparable to interobserver variability for clinical target volumes in the head and neck [54–57]. As more consistent and time-effective contouring is being realized, various commercial solutions are being released that offer DL-based tools for

Fig. 2. Automatable tasks in radiation oncology for the modern clinic. DT, dosimetrist/therapist; P, physicist; RO, radiation oncologist; AI, artificial intelligence/DL-based tool. The extent to which each skill set is used or task is performed in this figure is not indicated and may be dependent on each clinical practice. In order to group essential tasks performed during the treatment planning

process, “Physical,” “Knowledge,” and “Social” skill domains were created and are indicated by green, magenta, and blue ellipses, respectively. Skills or tasks are indicated by circles within each colored domain and may be shared between domains. Based on works cited in this review, tasks which may be automated are within the “Automatable” domain.

treatment planning. After Mirada offered automated contouring services (DLCExpert™) for autocontouring thoracic organs-at-risk in 2018, Raystation described its Deep-Learning Segmentation solution in a white paper in 2019 [58]. This tool allows the user either to access pre-trained UNET models for auto-contouring or allows the user to train a model with their own patient data. Such a process could move computational efforts off-line to allow for timely contours on multi-modality data (e.g., CT, CBCT, MR).

Other commercial vendors, such as Varian Medical Systems, are actively examining DL segmentation performance as a function of body site (e.g., breast, male pelvis, female pelvis), imaging modality (e.g., CBCT, CT), and training set size or diversity in patient population [53, 59, 60]. Ethos, Varian’s radiotherapy treatment system using AI and ML, provides an on-couch adaptive workflow for daily treatment [61]. Varian’s in-house trained segmentation model inputs the 3D CBCT and output segmentations of relevant organs using convolutional-neural-networks [61]. In addition to DL-based contouring, Ethos provides ML-based treatment plan generation to create an AI-guid-

ed system for adaptive radiotherapy [61]. The Ethos received a CE mark in September 2019 and 510(k) clearance from the FDA in February 2020. Also gaining attention is an AI-based treatment planning platform (Radiation Planning Assistant, RPA) developed by academic researchers and clinicians at MD Anderson Cancer Center [43]. The RPA is being designed to be accessible (via website: <https://rpa.mdanderson.org>) to any clinic in the world in need of high-quality contouring or treatment planning services. After registered participants perform a mailed dosimetry audit and treatment planning credentialing process, users can download automatically generated contours and treatment plans after uploading a patient CT and service request to a secure web server. Treatment plans for head and neck (VMAT), breast/chest wall (3DCRT), and cervical (3DCRT) cancers are examples of such services. DL and ML-based tools perform a majority of the contouring and quality assurance tasks, while dose optimization and calculation are automatically performed using the Varian Medical Systems engines [43, 62]. Considering that thousands of medical physicists and radiation oncologists are still needed in low- and middle-income countries [63], such a

web-based solution stands to increase access to services that may offset labor and resource deficits. However, accessibility to this treatment planning solution will depend upon each clinic's access to the internet.

While DL-based segmentation is a powerful tool, one challenge that customers or developers may face is providing hundreds of contoured datasets for training custom models. For such challenges, users may consider examining curated datasets that are freely accessible through The Cancer Imaging Archive [64] or other datasets noted by Shen et al. [13]. In addition to using freely available data, anonymization and sharing of well-curated datasets drive advancement and collaboration. Lessons may be learned from efforts to compile and share imaging datasets of patients with COVID-19 by those in industry, government, and academia in an effort to better combat the COVID-19 pandemic [65–67]. Other examples are grand challenges and DL competitions for medical image segmentation and classification, such as those offered through MICCAI, AAPM, and other organizations through <https://grand-challenge.org/>. Various organizations like the Cancer Imaging Archive or Creative Commons, offer services and/or licenses for data sharing.

Skills, Jobs, and Technological Change

As accessibility and adoption of DL-based technology increase over the next several years, many treatment planning tasks in radiation oncology will become increasingly automated or transformed. Because workers may either be augmented by new technology or in competition with it [68], it is important to consider what skill requirements may change for dosimetrists, physicists, and radiation oncologists. As noted by Frank et al. [68] in their article discussing the impact of AI on labor, “the skill requirements of each job title are not static and actually evolve over time to reflect evolving labor needs”. If employers can anticipate how future skill and labor requirements change with adoption of DL-based tools, skills that may be removed from competition with technology can be identified and skills that are useful for other essential tasks can be effectively harnessed. To provide insight into how departments may envision changing skill requirements amidst technological change from AI, we have mapped relationships between roles and skills within radiation oncology treatment planning. Using compiled surveys [69], professional documents [70–73], and career resources [74], we present potential skill intersections between AI and humans (Fig. 2).

For the purposes of this review, tasks will be defined as an activity having a beginning and an end. A skill is de-

finied as the capability to perform a certain set of tasks. In order to create a mapping which is generalizable and informative, roles such as the research assistant, engineer, physics assistant, and radiation oncology resident are not included. In addition, due to the dynamic role of the dosimetrist and therapist in other countries and clinics, the therapist and dosimetrist were combined into one role. One assumption made by this figure and this article is that social domain skills and tasks are not automatable, require human-human interaction, and are performed by all on the treatment planning team.

Because technology-intensive fields change rapidly over time, tasks performed in these fields also change. Whether or not roles will be removed in the decades to come is uncertain. However, after the clinical adoption phase is completed and technologies are soundly incorporated into practice, gains in efficiency from DL-based tools may augment the tasks performed by each member of the treatment planning team and allow for more time to perform other tasks. According to a compilation of surveys by Kisling et al. [69] in 2018, medical physicists on average spent 87% of their time performing “clinical service and consultation,” 7% of their time performing “research and development,” and 5% of their time “teaching.” Given that most respondents (>90%) perform plan review and weekly chart checks [69], physicists may spend a larger portion their time in the future on non-automatable tasks such as quality improvement, FMEA, research, or teaching (given that clinical workload remains constant). As suggested by Tang [9], the physicist may find that he or she has more time to perform tasks that are considered to be “non-routine” activities (e.g., commissioning, implementing new technology, and patient-specific consultations). Also important for the future workforce, as noted by Atwood et al. [75], may be a more direct role in patient care responsibilities, such as a physicist-patient or technical consult. As noted by their phase-II clinical trial, such changing roles may allow for patient anxiety and satisfaction to be better understood.

With the changing role of the medical physicist in mind, it is likewise probable that skill and task refocusing may occur for dosimetrists and radiation oncologists. With increasing access to and adoption of deployed AI tools, clinics may see the total time commitment from routine to non-routine activities shift if contouring and planning are completely automated. Also important to note is that in addition to DL-based tools, time savings from other tasks in treatment planning have been realized through scripting and other automated treatment planning tools reviewed by Wang et al. [19].

Fig. 3. Change in task and time allotment as a function of increasing access to AI tools. As access to deployed AI tools increases, members of the treatment planning team may experience changes in time commitment due to time and efficiency gains from AI tools. Routine tasks (magenta) requiring large time commitments to manual tasks may decrease, while time commitments to non-routine (blue) tasks may increase. Such changes can positively benefit practice.

Instead of contouring (organs at risk or targets), radiation oncologists may spend more time on patient consultation, teaching, and research. For the dosimetrist, the time efficiency gains from automated contouring and planning may be spent on clinical trial enrollment and special procedures. In these instances, more time for less urgent tasks may be a benefit of DL-based tool adoption (Fig. 3). Other potential benefits include increases in quality, safety, standardization, and compliance. Through further inspection of Figure 3, it is noted that while the urgency of tasks will not be affected by adoption of these tools, the time commitments to certain tasks may change. For example, less time may be spent on treatment planning, while more time may be spent on research or process improvement measures like FMEA (Fig. 3). For clinics with staff or resource shortages, time savings from using such tools may help to decrease the burden from heavy clinical workloads, improve throughput, and allow integration of more complex and time-intensive treatments. This may be a source of significant impact on a global scale, as many low- and middle-income countries suffer from lack of resources and staff [63].

The potential impact of automation on job security and interest in both medical dosimetry and medical physics are important considerations. Of note, the expecta-

tions for growth in oncology-related careers as the population ages and global cancer cases rise [76] suggest that there is in fact a bigger risk of understaffing for these professions in the coming decades. In fact, Lenards [77] analyzed recent medical dosimetry graduates and found a 100% job placement rate. Hence, the daily job tasks of medical dosimetry and physics professionals may be altered by the integration of automated techniques, but with the growing burden of cancer, this may allow us to keep up with the patient care needs in a more efficient way (not obviate the positions or careers).

Conclusions

Based on economic forecasts and trends from both academic and commercial developments, AI is evolving within the radiation oncology clinic. How AI has emerged, and how it will continue to progress, has been examined within the context of past technological advancements in radiation oncology. Compared to past transformative innovations, such as the Monte Carlo method or IMRT, the development and adoption of DL-based tools is occurring at faster rates and promises to transform practices of the radiation treatment planning team. Based on hype curve

predictions, approximately 20% of clinical practices may be using DL-based tools clinically within the next few years. As discussed, many vendors offer DL-based tools. However, accessibility to these tools may be determined by each clinic's ability access to the internet or obtain high-performance computing hardware. As seen by the trends exhibited by many technologies, high dependence on new technology can result in harm should the product fail in an unexpected manner, be misused by the operator, or if the mitigation to an expected failure is not adequate. Thus, the need for users to understand how to operate tools appropriately, for professional bodies to develop guidelines, and for manufactures to participate in regulatory efforts is essential. Given that members of the radiation treatment planning team perform many tasks that are automatable, the use of DL-based tools, in combination with other automated treatment planning tools, may refocus tasks performed by the treatment planning team and may potentially reduce resource-related burdens for clinics with limited resources.

Conflicts of Interest

Multiple authors of this publication are members of the Radiation Planning Assistant team at the University of Texas MD Anderson Cancer Treatment Center.

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Author Contributions

All authors contributed to the conceptualization, writing, and editing of this work.

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