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Review

Advances and future of Radiation Oncology

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ABSTRACT

Aim: Review of recent advances and vision for future developments in clinical practice of Radiation Oncology.
Background: There have been substantial research and technological developments in Radiation Oncology over the past 40 years.
Materials and methods: The relevant literature was reviewed and the authors offer their perspective on future opportunities for advancement in Radiation Oncology.
Conclusions: Significant innovative technological developments have been introduced in the practice of Radiation Oncology, with more precise target delineation and tracking and three dimensional treatment planning, optimal delivery of radiation therapy to the target and lower doses to surrounding Organs at Risk. This dose optimization and adaptive therapy have enhanced the role of Radiation Therapy to more effectively treat patients with cancer. Further creativity and refinements will continue to advance the field into new applications of ionizing radiations in cancer therapy.

1. Introduction

Radiation Oncology is one of the pillars of multidisciplinary care of the patient with cancer. In the past 50 years, and especially the last 20, Radiation Oncology has experienced dramatic technological innovations (Fig. 1), leading to image-based complex three-dimensional treatment planning and delivery of radiation therapy, using 3D-Conformal or Intensity Modulated Radiation therapy (IMRT), with increased precision in dose delivered to the target volume(s), while sparing adjacent normal structures (Organs at Risk, OAR).[1] The dose-rate effect of external beam radiation therapy with conventional linear accelerators is governed by the overall beam-on-time. With the advent of flattening-filter-free accelerators and hypofractionation (high dose per fraction) radiation therapy schemas, biological effects of external beam dose rate will need further investigation.[2]

2. Treatment planning and dosimetry

Requirements on dose conformality, smaller PTV margins and the sharp peripheral dose gradient of these techniques require a more stringent Quality Assurance Program. Widespread use of electronic clinical and dosimetry records and informatics methodology will add reliability to the data acquired. Exponential growth of medical imaging modalities (CT, MRI, US), including image fusion have enhanced our ability to diagnose cancer at earlier stages and to more accurately stage the tumor. The improvement in staging accuracy has enabled us to better tailor therapy based on the characteristics and

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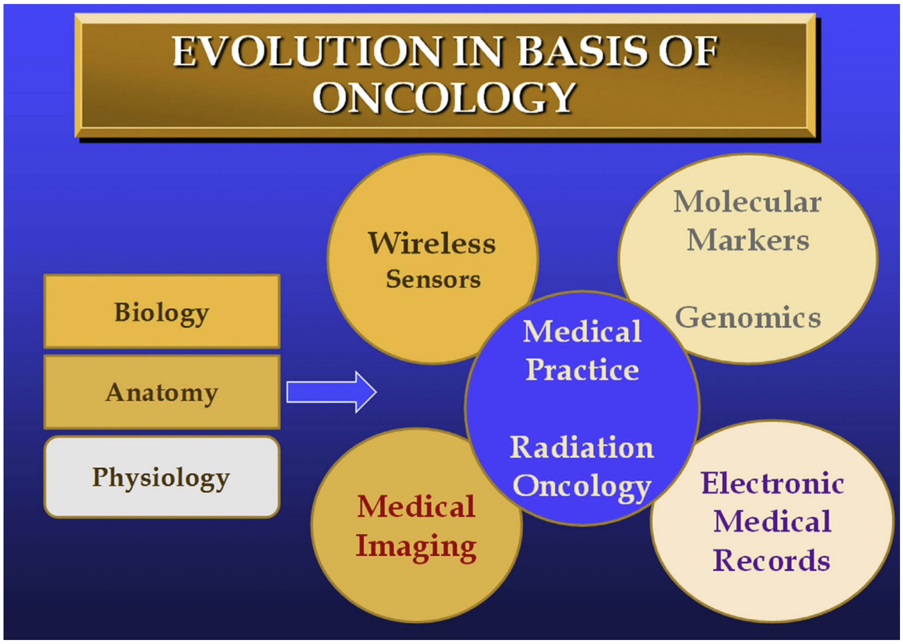

Fig. 1 – Evolution in basis of Radiation Oncology.

the extent of the individual patient's tumor. In the past 10 years there has been an increasing use of functional PET imaging (18F-FDG or other specific radiotracers for hypoxia, cellular proliferation, angiogenesis, etc.) or magnetic resonance spectrometry, with better delineation of target volumes, particularly clinical target volumes.[3]

3. In-Room imaging

In-Room on-line imaging devices, including Cone-Beam CT (CBCT), commercially available have facilitated the implementation of Image-Guided Radiation Therapy (IGRT). Implanted target tracking devices enhance our ability to more accurately localize the target for treatment. 4D CT scanning with faster scanners and treatment planning has facilitated correction of target motion in the lung and upper abdomen, including Active Breathing Control Techniques. As a corollary, stereotactic hypofractionated techniques have been introduced in the treatment of brain, lung, and tumors in other anatomical sites.

While the CBCT and these other technologies have come a long way, we are still unable to image and quantify the true extent of soft tissue tumors on daily basis and during the radiation delivery. This undoubtedly remains one of the last frontiers in Radiation Oncology and the recent technological developments and research indicate that we will have these capabilities in the upcoming years. Internal implantable electromagnetic or transmission dosimeters may eventually facilitate the verification of actual radiation dose administered to the target and OAR.

As to the future, we envision an active role of Radiation Therapy in combination with cytotoxic or biological agents. While the effect on the tumor may be enhanced, so will be the sequelae in OAR. This will require more rigorous treatment planning and Quality Assurance, to diminish toxicity and unintended radiation effects.

4. Molecular biology and genomics

The application of genetic profiling and DNA mapping, already used by Medical Oncologists to select patients that will respond to a specific antitumor agent or to protect normal tissues may eventually be introduced in the practice of Radiation Oncology.[4] A Holy Grail of research in Radiation Oncology is the identification of specific genes or molecular markers to both to predict response of tumors or normal tissues to a prescribed dose of irradiation.

For the past 50 years in some tumors combinations of cytotoxic agents and radiation therapy have improved outcomes in many patients. In the future combining genetically engineered biological agents or molecular compounds may enhance the effects of radiation therapy on some cancers.

Regardless of the radiation modality we must strive to optimize dosimetric precision, in radiation treatment planning, delivery and verification. One of the key elements in delivery of radiation therapy that is still to be attained is accurate assessment of the true dose, D_A, delivered to the patient. Despite all of the advances in treatment planning, imaging, and delivery, the true impact of dynamic nature of cancer patients (inter and intra fraction motion and patient changes) remains unknown for the majority of radiation therapy patients.[5] The existing and upcoming developments including: fast image acquisitions for daily treatments as well as during the actual radiation delivery, auto contouring and deformable contour propagation, and fast dose calculations will enable much better quantification of the D_A. The knowledge of D_A will enable further optimization of tradeoffs between doses delivered to tumor volumes and those delivered to Organs at Risk. A better understanding of the limits for these tradeoffs will enable exploration of the true limits of radiation therapy effectiveness and will guide future developments in technology and procedures.

5. Future advances

Medical Imaging will continue its vertiginous progress with additional refinements, molecular approaches and more specific radiotracers or radiopharmaceuticals are being developed to identify distinctive tumor characteristics that will translate into more accurate target delineation and enhanced radiation treatment planning and delivery. Computer technology will continue to grow exponentially[6] and to accommodate expanding loads of imaging and computational dosimetry data more reliance will be placed on cloud computing. Among the benefits of cloud computing are standardization, faster rate of technology adoption, promotion of best practices as well as potentially significant cost savings.

Because of existing interobserver variability in target and even OAR delineation it will be important to standardize image acquisition and interpretation criteria by Radiation Oncologists and Diagnostic Radiologists and foster training in this field. This persistent interobserver and interpractitioner variability despite the continuous improvements and standardization in diagnostic and technical capabilities is accelerating the need and research in decision support and knowledge based tools. While such tools have had a varying degree of acceptance in other areas of medicine, they are still in infancy in Radiation Oncology and will likely become one of key clinical and technical areas of interest. This need is further fueled by the much more ubiquitous availability of the most advanced technologies in areas which historically would not have been able to afford such technology. Due to economic globalization now these areas and countries can afford the latest technologies but it will take some time for them to be able to create professional and technical staff which can take the full advantage of these technologies and decision support and knowledge based tools can significantly accelerate bridging of this gap.

Heavy particles and protons, already in clinical use in many countries will continue to expand. It will be critical to establish the potential cost benefit of these modalities and identify the selected group of patients to be treated with them.

6. Adaptive radiation therapy

Whereas radiation dose escalation is attractive and in some sites it has been shown to improve tumor control (i.e. prostate cancer), the new technological developments are particularly attuned to the use of hypofractionated, including stereotactic irradiation, which has not only biological rationale but ideally an impact on resource utilization and the cost of patient care and convenience. The above advances in computational capability and electronic engineering will amplify the opportunities to administer Adaptive Radiation Therapy on a real-time basis, to daily optimize dose, to accommodate anatomical deformation or changes in the volume, configuration or biological tumor characteristics using automated segmentation and to correct random or systematic positioning uncertainties. We envision further refinements in designing more versatile and reliable software, remote computational techniques and automation for treatment planning and delivery, to enhance efficiency and safety in the processes of radiation therapy. Further, the voluminous amount of clinical and dosimetry data generated with contemporary techniques requires a robust processing system, which in the future will be strengthened with refined informatics and use of cloud computing for data acquisition, analysis and storage. The advances in speed and scope of imaging technologies used in radiotherapy, will allow us to quantify anatomical and biological characteristics of patient anatomy at an increased frequency and some aspects of this is already used for daily patient assessments and the scope of these assessments will continue. It is also likely that there will be a continuation in increase of image acquisition during the actual treatment delivery. These evolutions in imaging capabilities coupled with fast contour delineation and fast dose computation should allow us to more adequately quantify true doses delivered to target volumes and normal structures and to quantify their response treatment. The increased availability of such technology along with cloud based infrastructure should also accelerate the implementation of these processes for a large number of patients.

7. Brachytherapy

Brachytherapy, prime exponent of adaptive radiation therapy, will incorporate many of these advances in the management of suitable patients.[7] Other more exotic area with potential application in clinical Radiation Oncology is the use of nanoparticles with specific target radiotracers for imaging or radiopharmaceuticals for therapeutic purposes.[8]

8. Cost benefit and Comparative Effectiveness

Because of growing concern world-wide with the ever-increasing cost of health care and of sophisticated new technology we will need to increase our efforts in using cost benefit and comparative effectiveness techniques to document the gains that innovative technology may provide in patient care.

9. Need for refined quality assurance

Complex technology is associated with a potential increased risk on unintended undesirable effects. We must remain extremely vigilant and continuously establish and apply in our daily practice Quality Assurance Programs that will ensure the safety of our patients (and colleagues) and enhance the precision in planning and delivery of radiation therapy, as well as the reliability of data in clinical trials.[9–11]

Conflict of interest statement

None declared.

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