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An Overview of Technological Developments in Medical Applications of X-Rays and Radioactivity

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Abstract

The years 1895 to 1898 were momentous for their impact on health and human well beings. First, Wilhelm Roentgen noted a glowing fluorescent screen, caused by invisible rays. This event subsequently led to the discovery of X-rays in 1895, and thus the birth of the "atomic age". Next Becquerel's investigations of these mysterious rays led to his experiments with uranium salt crystals. He thought that when these crystals are exposed to sunlight they could emit rays and cause exposure on photographic plates. This led to the discovery of radioactivity in 1896, with its full significance appreciated when the Curies discovered radium in 1897. The term "radioactivity" was first used by Marie Curie to describe this phenomenon that led to the birth of the "nuclear age". Shortly after, the medical applications of x-rays and radioactivity were recognized and widely disseminated.

In the past 100 years, the technological developments in the production of x-ray beams along with the impact of the discovery of artificial radioactivity by Irene Curie and Frederic Joliot in 1930s have revolutionized the practice of medicine. Currently x-ray imaging is being used, more than any other imaging modality, in diagnosis of diseases and abnormalities. In addition, over 50% of all cancer patients receive radiation treatments as part of their treatment plan(s). Despite significant advances in imaging technology and in production and delivery of x-rays and radioactivity, about half of these patients are successfully cured with 5 to 10 years local control. Reasons for treatment failure with radiation may be several including physical, biological, or both. For example, because of the imaging limitations, the exact extent of disease for many tumors is often unknown. Moreover, some tumors are able to "repair" radiation damage very effectively and some are radio resistant due to relative hypoxia.

In recent years, the major "challenge" of radiation treatment is to deliver large enough doses to the most resistant cancer cells to provide a high probability of local control while minimizing the dose to normal tissues and hence reducing complications. With recent developments in "imaging" the metabolic or functional status of cancers, the position of tumors relative to surrounding normal tissue can be more clearly delineated. The therapeutic dosage of radiation to the tumors can be escalated without exceeding normal tissues tolerances. These special techniques include: 3D "conformal" radiation treatment where the shape of the high dose region "conforms" to the shape of the tumor ("target"), intensity modulated radiation therapy (IMRT) that uses combinations of radiation beams with varying spatial intensity across the fields ("intensity modulated") in order to achieve an "ideal" dose distribution, image guided radiation treatment, and heavy charged particle radiotherapy. As such, it is expected to increase the success rate of cancer treatment significantly with this radiation treatment modality.

Keywords

Medical Applications, X-Rays and Radioactivities, Conformal Therapy

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Introduction

In the last few years of the 19th century three major discoveries had great impacts on health and human well-beings. These were the discoveries of X-rays by Wilhelm Roentgen in 1895, followed by the discovery of radioactivity by Henri Becquerel in 1896, and the discovery of radium by Pierre and Marie Curie in 1898. Soon after these discoveries medical applications of X-rays and radioactivity were recognized [1].

In the past 100 years, the technological developments in the production of X-ray beams along with the impact of the discovery of artificial radioactivity by Irene Curie (daughter of Marie and Pierre Curie) and her husband Frederic Joliot in 1934 have revolutionized the practice of medicine. At present, X-ray imaging is being used, more than any other imaging modality, in diagnosis of diseases and abnormalities. In addition, over 50% of cancer patients receive radiation treatments as an indispensable part of their treatment plan [2].

Over the past 100 years major advances in imaging include but not limited to Computerized Tomography (CT), Single Photon Emission Tomography (SPECT), Positron Emission Tomography (PET), and nuclear Magnetic Resonance Imaging (MRI). Currently the most common imaging techniques in detection and diagnosis of disease and abnormalities are: X-rays, radioisotopes, and MRI.

Likewise, in the past 100 years, major technological advances have occurred in the therapeutic applications of X-rays and radioactivity. These major developments include (but, of course, not limited to) Co-60 teletherapy units, linear accelerators, Low Dose Rate (LDR) radioisotope therapy known as brachytherapy, and High Dose Rate (HDR) brachytherapy. Currently, over 50% of cancer patients receive X-ray and radioactivity as part of their treatment plan(s). However, only (about) half of these patients are successfully cured with 5 to 10 years local control.[?] Reasons for treatment failure with radiation may be several including physical, biological, or both. Since all the imaging techniques have their own limitations, the exact extent of disease for many tumors is often unknown. In addition, some tumors are able to "repair" radiation damage very effectively and some are very radio resistant due to relative hypoxia. These issues are now being addressed over the past 10 years or so.

At present, the major "challenge" of radiation treatment is to deliver large enough doses to the most resistant cancer cells to provide a high probability of local control while minimizing the dose to normal tissues and hence reducing complications. With recent technological developments in imaging such as functional MRI (fMRI), the metabolic or functional status of different types of cancer and disease abnormalities as well as the position of tumors relative to the surrounding normal tissue can be more clearly delineated. As a result, the therapeutic dosage of radiation to the tumors can now be escalated without exceeding normal tissue tolerance. These special techniques include ,but not limited to: 3 dimensional (3D) conformal radiation treatment where the shape of the high dose region conforms to the shape of the tumor (target), Intensity Modulated Radiation Therapy (IMRT) that uses combinations of radiation beams with varying spatial intensity across the fields in order to achieve an ideal dose distribution, image guided radiation treatment, and heavy charged particle radiotherapy. With these technical developments, the success rate of cancer treatment is expected to increase significantly.

One of the major challenges in medical applications of X-rays and radioactivity is to deliver large enough doses to most resistant cells in order to increase the probability of local control while dose to normal tissues are kept low enough to minimize the probability of complications, that is to maximize the

Probability of Uncomplicated Local Control (PULC). Unfortunately, the outlook to achieve such a goal is not quite promising.

Furthermore, the PULC is increased with 3D treatments where the shape of the high dose region(s) confirms to the shape of the tumor (i.e. target), IMRT that uses combination of radiation beams with various weighting factor(s), image-guided radiation treatments that often employs X-rays, and HDR. With all these techniques, it is extremely important to know the exact position and extent of the tumors. However, since many tumors are indistinguishable from surrounding normal tissues, it is possible to see them by fusion of CT and PET (PET/CT), CT and MRI (CT/MRI), and Magnetic Resonance Spectroscopy (MRS) images.

Moreover, it is worth noting that conventional radiation treatments are often attained by radiation beams of constant intensity (or by uniformly varying intensity) in one direction. With conventional radiation treatments, dose distributions are calculated after all the radiation beam parameters such as number of fields, and directions of beams are specified. This is often referred to as forward treatment planning. However, radiation dose distributions can be improved if the radiation beam intensities are varied in two or three dimensions as it is done in IMRT technique. At present, IMRT radiation treatment technique is often accomplished by linear accelerators that emit high-energy X-ray beams and utilize multileaf collimation. With IMRT radiation treatments, the radiation oncologist specifies the desired dose distribution for each patient. The computer determines how *best* to achieve this by adding IMRT parameters. This procedure is often referred to as inverse treatment planning.

It should be noted that a major problem with IMRT is ensuring that the patient is positioned quite properly when undergoing radiation treatment. Since IMRT is highly conformal any small misalignment might miss part of the tumors. One solution is to provide CT imaging as an integral part of the linear accelerator assembly as it is done with Tomotherapy units. For these units, the accelerator provides X-rays for CT imaging as well. The CT detector device that images the X-rays after transmission through the patient is placed directly opposite to the accelerator. Both the accelerator and the CT assembly rotate around the patient while the treatment couch moves longitudinally. With this treatment technique the radiation beam is continuously modulated by a special multileaf assembly – thus providing spiral scans for accelerator and CT and creating helical tomotherapy. Many believe that helical tomotherapy may well become the treatment of choice for many malignancies [Personal communication with Prof. Thomas Mackie, University of Wisconsin, Madison, Wisconsin, USA].

Another problem with conventional radiation treatments is that for each radiation beam, the dose in the patient decreases with depth due to absorption in the tissue. As a result, the dose to the tumor at depth is lower than the dose to the normal tissue through which the beam passes. The IMRT technique reduces this problem but does not resolve it entirely. With heavy charged particles that are heavier than electrons, the dose at depth is much higher than the dose to intervening tissues due to the Bragg peak. The depth of Bragg peak increases as energy increases. The narrow Bragg peaks in depth can also be modulated to cover the tuner at depth. One major feature of heavy charged particles is that they exhibit radiobiological advantage over X-rays because the impact of cell repair, hypoxia, and the cell cycle are reduced. Unfortunately, heavy charged particle treatment units are expensive and require high maintenance.

Finally, soon after the discovery of Radium (Ra), the use of Radium sources for brachytherpy procedures continued well into the 20th century. However, since the energies of the gamma rays emitted from Radium are very high, it is very difficult to shield them. The major challenge in medical applications of radioactivity is to deliver *adequate* dose to the patient while maintaining exposure to the individuals near the patient to acceptable levels.

With discovery of artificial radioactivity in 1934, the use of Radium sources were gradually replaced by ^{137}Cs, and more recently by ^{192}Ir. Even with these isotopes, exposure to the personnel during placement of the sources in the patient and during the following days that the patient is being treated is very high. This type of brachytherapy that is also known as LDR was gradually replaced by HDR remote after loading units. With HDR units such as GAMMAMED, source intensity is about 1000 times higher than that used for LDR and the treatment time(s) are much shorter and are remotely controlled by a computer. These sources are kept inside well-shielded assemblies and the patients are treated inside well-shielded treatment rooms after appropriate catheters and/or applicators are placed in the patients. In HDR procedures, the source positions and dwell times can be varied in order to maximize tumor (target) dose while minimizing doses to normal tissues. However, since the half-life of ^{192}Ir is about 74 days, the source needs to be replaced about every three months; otherwise, treatment times become long. Thus brachytherapy with these units are expensive and require high maintenance.

In conclusion, Technical developments in medical application of X-ray and radioactive sources over the past decade have brought a number of exciting new technologies for imaging and treatment of cancers and human abnormalities. However, these technological developments have been very costly. Their limitations in imaging and their efficacy in treatment are being questioned and examined by many scientists.

References

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