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DEVELOPMENT OF CONTEMPORARY CLINICAL ONCOLOGY THROUGH THE INTEGRATION OF MEDICAL PHYSICS

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Abstract:

Object: We see that contemporary clinical oncology is actively developing due to the fact that new diagnostics and treatments are being introduced that are based on physical processes. Radiology, hyperthermia, cryology, as well as photodynamic therapy, ultrasonic cavitation, information technologies are currently actively developing [1]. We must not forget that medical physics itself generates the development of new technologies.
Biologically, current oncology implies a staged, abrupt development of the tumor process. The periods of development of a malignant neoplasm highlight certain characteristics that make it possible to target the methods of diagnosis and treatment of a tumor [1].
The problem is not only the treatment of neoplasms by destructive surgical removal or irradiation with severe sources in high doses, accompanied by a violation of anatomy and function of organs, disability of patients but also a pointed, selective effect on small cancers or precancer, implementing the principle of organ-preserving, functionally sparing treatment of tumors of the clinical oncology general concept.

Methods: Having analysed scientific articles on the topic of the use of photodynamic therapy, radiation therapy, which in recent years have made significant progress in their development.

Findings: Physical technologies are currently often used in the treatment and diagnosis of oncology. Information technologies are also involved, which are used in medical instrumentation, these are both smart surgical lasers, which are directly related to the surgeon, and streoligraphy (diagnostics).

Conclusions: Thus, we determined that the active development of clinical oncology would not have been possible without such a component as medical physics. Due to its integration into this area, it has been filled with new methods and methods of diagnosis.

Keywords: oncology, medical physics, diagnostics, radiation oncology, photodynamic therapy.

INTRODUCTION

Cancer diseases are in the leading positions in the world in terms of mortality; and the dynamics show that there is no need to expect a reduction in patients in the coming years; the dynamics will only grow. This means that the priority task is to develop the diagnosis and treatment of cancer through the integration of medical physics into this industry in particular. That will enrich clinical oncology with more advanced methods and ways of diagnosis and treatment.

In recent decades, physicists have created and constantly improved a number of radiological complexes for diagnostics and therapy in clinical medicine.

These are radionuclide and accelerator complexes for external and internal radiotherapy, radiation scalpels (gamma knife and cyberknife), equipment for stereotaxic irradiation, tomotherapy systems, intraoperative radiation therapy systems, interventional radiology, X-ray or Computed Tomography (CT), magnetic resonance (MRI), single-photon (Single Photon Emission Computed Tomography (SPECT) and SPECT/CT), positron emission (PET, PET/CT and PET/MRI) tomography, PET centers and radionuclide therapy (RNT), proton (PLT), ion (ILT), neutron therapy, etc. [2]

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Rather wide range of radiological technologies, equipment and radiopharmaceuticals is already used for the diagnosing and treatment of oncological, cardiological and other serious socially significant diseases.

Radiology offers great diagnostic and therapeutic opportunities. This is an early diagnosis, accurate quantitative control in diagnosing and a controlled selective non-invasive therapeutic effect, sparing organ-preserving treatment and a high quality of life.

Medical physics has made significant contributions to recent advancements in radiation oncology. Medical physicists are key figures in clinical and scientific radiation oncology due to their unique skills, flexibility, clinical involvement and intrinsic translational nature. The continued development and widespread adoption of 'high tech' radiation therapy has led to an increased demand for the involvement of medical physics.

In this article, we have identified four main objectives of medical physics in radiation oncology:

1) object volume determination improvement;
2) introduction of artificial intelligence and automation;
3) development of models for predicting biological effects for precision medicine;
4) need for leadership;

New views and proposals of medical physics for the successful solution of these new problems are generalized. We foresee that scientific and professional problems of our time are pushing medical physicists to accelerate the transition to multidisciplinarity.

Medical physicists will hold down a crucial and key role in the assurance of quality, safety, and management of increasingly complex technologies. New challenges will require medical physicists to continually update their skills and innovations in education, adapt curricula to include new areas, and strengthen interdisciplinary relationships and a spirit of innovation. These challenges require forward-looking and open-minded leadership that can combine established roles with exciting new areas in which medical physics must increasingly contribute.

Radiation medicine began with the discovery of X-rays and radioactivity in the late 19th century, leading to the diagnostic and therapeutic uses of radiation. Several Nobel Prizes in Physics and Chemistry are part of the history of medical physics in visualization and therapy, therewith, Wilhelm Roentgen and Marie Curie are considered by many as the 'founders' of the application of physics in medicine.

Quite recently, the Nobel Prizes in Medicine have been awarded to physicists for their achievements, such as discoveries concerning the molecular structure of the deoxyribonucleic acid (DNA), the development of computed tomography (CT), or discoveries regarding magnetic resonance imaging (MRI). Physicists from the first applications of the late 19th century were involved in radiation oncology; and by 1912-1913, the first physicists were appointed to hospital positions (in Munich and London) [1]. Academic positions in medical physics also emerged early, for example, Sidney Russ was the first Head of Chair of Physics at London Medical School in 1920, or Rolf Sievert was appointed as a professor of Medical Physics in 1941 in Stockholm.

Thereafter, medical physicists have contributed to the technological and clinical advancements in radiation therapy and constitute a key profession that performs a central role in the interdisciplinary approach to cancer care facilities [2], [3]. Today, medical physicists have a responsibility (in cooperation with the other professionals) for ensuring the safe and optimal use of technology in medicine; their flexibility, clinical involvement, multidisciplinary nature, and unique skills are well known and appreciated both scientifically and clinically, in particular in radiation oncology. Another key point relates to the diverse 'work profiles' in medical physics, covering clinical service, academic circles and research, clinical development and adoption, and industrial research and development. This diversity is essential to medicine and, in particular, for radiation oncology.

The continuous development and widespread use of 'high-tech' radiation therapy in recent decades have led to an increased involvement of medical physicists [2], [3], [4]. Currently, radiation oncology has undergone changes, following the current evolution towards the era of 'exact oncology' [5]. These developments have provoked debates in the radiation oncology physicist community regarding the redefinition of the roles and responsibilities of medical physics in these new scenarios [2], [6].

MATERIALS AND METHODS

The research materials were scientific articles of domestic and foreign experts in the field of application of medical physics in the treatment and diagnostics of oncology.

We carried out a bibliographic analysis of available sources to determine the level of development and integration of medical physics into clinical oncology.

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LITERATURE REVIEW

With the ever-improving knowledge of tumor spread, the determination of the clinical volume of the target is still subject to great variability between and within observers [7], [8]. In other words, delineation of the clinical scope of a target can still be seen as an art professionally performed by clinicians in the literal sense of the word, intended as 'a skill acquired by experience, study or observation'.

Therefore, there is a significant potential to reduce the uncertainties in delineation of the clinical volume of a target using an evidence-based approach followed by medical physicists. Some evidence suggests that patients are over-treated due to the use of too wide boundaries of the clinical target volume [9]. For example, the inclusion of local regional lymph nodes for routine nodes irradiation often results in a multiple increase in volume [12], which has a negative impact on surrounding healthy tissue and unclear survival advantage for some tumor sites such as the breast and prostate [13], [14].

In spite of the significant recent advancements in visualization, microscopic expansions of the total tumor volume will remain invisible, as even advanced visualization techniques are unlikely to achieve the spatial resolution required to detect a few or separate cells. In exactly the same way, the lymphatic spread can remain invisible and undefined. Moreover, the interaction of different treatment methods, which is becoming the standard of treatment for some tumor sites, is insufficiently studied. Systemic treatment can be effective with microscopic disease and can reduce the need for expansion of the clinical volume of the target [15]. The role of the clinical target volume needs to be redefined, for example when considering synergistic effects of radiation therapy and immunotherapy [16].

Physicists can help in dealing with these serious problems from multiple angles:

1) First and foremost, it is important to collect and combine data such as broadened functional visualization and other biomarker data to better characterize the characteristics of tumor spread, including lymphatic spread and tumor/patient interactions. It has been shown how macroscopic magnetic-resonance imaging (MRI) can provide microscopic characteristics of the tissue [17], [18], [19], [20], [21]. It is also important to include longitudinal data, i.e., changed over time. Physicists, inter alia, need to ensure that the data is searchable, accessible, compatible, and reusable. When data is not available, physicists should be involved in collecting new data through clinical trials that are designed in a similar way to physical experiments and that can challenge clinical practice, for example, by significantly reducing the boundaries of the clinical volume of target.

2) Medical physicists, in collaboration with the biologists and biophysicists, should study models of channels of tumor expansion [22], as well as the effect of the combined therapies on the microscopic spread of disease, for example, the interaction of radiation and immunotherapy [23].

3) The progress in developing a framework for probabilistic determination of the clinical volume of the target is crucial [24], [25]. The standard binary definition (tumor/no tumor) does not reflect the underlying probabilistic nature of the problem. A probabilistic approach to CTV detection requires the integration of visualizing biomarker data (e.g., radiomics), relapse patterns, pathology data, decreasing volume clinical trial data, and tumor probability maps to quantify the risk of marginal recurrence and balance competing risks.

4) The first steps forward will be the implementation of the most recent agreed guidelines for the clinical volume of target and, for example, for the automatic expansion of a visible tumor while observing anatomical barriers to tumor expansion. Approaches need to be developed and can be tested at specific disease sites such as the head and neck, lungs, and central nervous system.

The potentials of modern oncology have expanded significantly with the appearance of **photodynamic therapy (PDT)**.

Photodynamic therapy is a fundamentally new method of malignant neoplasms treatment, based on the use of photodynamic damage to tumor cells during a photochemical reaction**.**

For the present, three main mechanisms of the antitumor effect of PDT are being considered - direct damage to tumor cells, disorder of the vascular stromal tumour, and elimination under the effect of the immune cells. An important factor in the induction of a PDT-mediated immune response is damage to cell membranes and vessels of the tumor.

Areas of intended use:

— skin cancer;
—melanoma and breast cancer intracutaneous metastases;
— tumors of the oral mucosa, the mucous membrane of the tongue, lower lip;
— laryngeal tumors;
— tracheal tumors;
— bronchial tumors;
— tumors of the esophagus;

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— tumors of the stomach;
— rectal tumors;
— tumors of the genitourinary system.

The main disadvantage of photosensitizers is their long-term retention on the skin surface. Even at the lowest concentration of photosensitizers in the skin, they determine the increased sensitivity of the skin to light and phototoxicity.

The result of the clinical manifestation of this phototoxicity in case of the failure to comply with the light regime can be the first-degree burn of the skin of the face and open areas of the body, followed by pigmentation.

With multiple and extensive tumor nidi, especially ulcerated ones, and a violent photochemical reaction with extensive necrobiotic processes, a hyperthermic reaction and intoxication are possible due to the absorption of decay products.

Edema in the next day after the PDT session, as a manifestation of a photochemical reaction in tissues due to interstitial light scattering, is observed more or less in almost all the patients. It is especially pronounced in PDT of the facial skin. This edema does not require special treatment and disappears on its own in 3-4 days after the radiation session.

With PDT of esophageal cancer, the development of esophagitis is possible, and with an overdose of radiation, the formation of a circular cicatricial stricture in the long term is also possible.

PDT method compares favorably with traditional methods of malignant tumors treatment (surgical operation, radiation, and chemotherapy) by the high selectivity of the lesion, the absence of the risk of surgical procedure, severe local and systemic complications of treatment, the possibility of multiple repetitions, if necessary, of a therapeutic session and the combination of fluorescence diagnostics and treatment in one procedure. impact. In addition, one course of PDT is sufficient to eliminate the tumor in most patients. [27]

Development and implementation of artificial intelligence in radiation oncology

Artificial intelligence (AI) solutions are currently entering this area of application for a number of applications [28], awaiting impact at the professional, healthcare system, and patient levels, including improved access to treatment. These decisions must follow the same technology adoption process as other engineering principles have an application to medicine [31].

Firstly, a clinically unmet need or problem is identified and defined, where new solutions are proposed based on the proposed requirements; this is followed by a variation stage to test whether the new solutions comply with standards for use in clinical practice; before finally making it easier for end-users (e.g. clinicians, radiation therapists, medical physicists) to understand the principles of AI that are critical to successful and safe implementation into the clinical practice.

The following four key points are considered the main priorities of medical physics in this area:

1) Implementation and customization of AI technology. The long tradition of successful implementation of new technologies mainly arises from a collaboration between medical physicists and therapists, nurses, and technologists. This environment provides medical physicists with a unique opportunity to contribute to the introduction of AI into the clinical environment together with AI specialists [28]. Thereby, medical physicists must now expand their space of collaboration and work together with scientists and data scientists to safely and effectively implement AI into current patient care. It starts with an understanding of the technology currently in use.

2) Development of AI technology. Physicists are attracted to perform a central active role in the forthcoming field of artificial intelligence, and they are contributing to defining the directions that need to be taken to ensure appropriate clinical implementation. Therefore, collaboration with industrial and research groups in the field of computing is of first-rate importance to access the latest technology and scientific knowledge. A simplified approach may consist of teaming up with data engineers to implement existing tools. However, application and interpretation must come from the very field of medical physics. The success of artificial intelligence approaches depends not only on the quality and quantity of data required for training but also on the ability to rephrase clinical questions for data engineers. Besides, collaboration with other disciplines is key to success.

3) Facilitation of access to correct data. The hospital IT environment is changing rapidly, and medical physicists must perform an active role in this to ensure access to data sources for AI development. Apart from advising on IT infrastructure requirements, medical physicists, together with physicians, are responsible for interpreting and developing appropriate models: for example, predictive models or more advanced solutions [31]. Data mining technology is just one aspect of this work, as there are also challenges to aligning different stakeholders (IT, physician, legal entity/patient privacy, etc.) seeking to collaborate and achieve a common (clinical) goal. Besides

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quantity, the quality (e.g. wealth, size, and quantity of curation) of datasets is of first-rate importance to the successful training and implementation of AI models in clinical practice.

4) Education and training of artificial intelligence skills. Apart from the implementation, discussion and interaction with industry are also required to introduce these new technologies with innovators and pioneers. Clinical medical physicists need the training to use these new developments, and commissioning and quality assurance programs need to be developed.

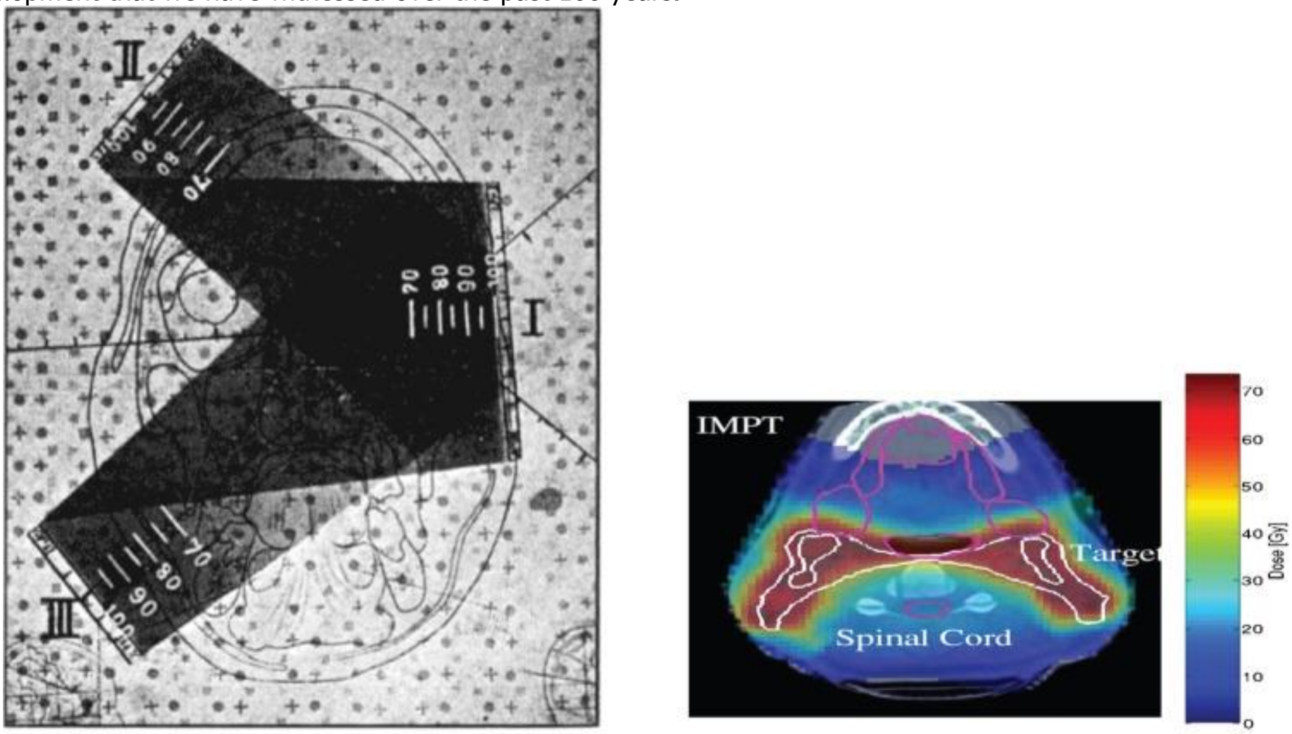
Radiation therapy

Radiation therapy would not exist without physics. Although radiation therapy 'exists' at the intersection of many disciplines, its dependence on physics is perhaps the strongest. By this, we mean not only dependence on clinical physics support to ensure safe and accurate administration of radiation, but above all dependence on scientific and research aspects of physics in general and medical physics in particular. We tend to think of medical physics as physics in medicine to emphasize the importance of physics.

The central area of focus of physics in radiation therapy has always been to improve the level of accuracy and precision in the administration of a dose to a target volume (tumor). Significant progress has been made in this area, based on four basic events:

- Fundamental discoveries leading to new treatments and visualization;
- Technological inventions in the administration of radiation doses;
- Technological inventions in treatment planning;
- Technological inventions in the field of image processing.

Considered all, the history of physics in radiation therapy is the history of improving the localization of dose in space and time. The progress made in this area is truly impressive. The medical physics mantra of concentrating the radiation dose in the tumor volume and the greatest possible preservation of the surrounding healthy tissue has been successful and has led to dramatic changes in how we plan, optimize and perform radiation therapy (Figure 1). It is now possible to administer a highly concentrated dose to a tumor with a spatial accuracy of 1–2 mm and a dosing accuracy of 2%. The healthy tissue dose has been significantly reduced through better geometric dose shaping and the use of advanced therapies, including proton and heavier particle therapy. Combining this with the radiobiological advantage of a differentiated ability to repair the damage between tumor and normal tissue, we are now in the position of providing radiation therapies that can clinically control the tumor while avoiding toxicity to normal tissues. All this would have been impossible without the phenomenal advances in fundamental physics and technological development that we have witnessed over the past 100 years.



(a) (b)

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Figure 1

100 years of radiation therapy development have changed the world for the better. Comparison of the X-ray treatment plan of the early 1900s (Figure 1 (a) from [8]) and the proton treatment plan of the early 2000s (Figure 1 (b), courtesy of A. V. Chan and A. V. Trofimov, MGH Boston).

The strong reputation of radiation therapy today is largely based on physical research from the past. The scientific method has performed an important role in this evolution over the past century. New challenges and opportunities await research-oriented physicists both in the traditional field of radiation therapy and beyond. However, the current focus on the professional side of medical physics away from research makes it difficult to meet these future challenges.

RESULTS

While medical physics is currently on the rise and it can be argued that there is nothing to worry about, further reflection reveals several problems that, if not properly settled, could lead to a diminution of the role, and then to the destruction and fall of the entire field of medical physics. We are starting to see negative symptoms from research. It is becoming increasingly difficult to find good research-oriented medical physicists at the postdoctoral level. Some reasons and possible solutions are discussed below. The research grants funding situation has become very tight due to the global economic problems, although some of the recent indications are more positive. There is a sense in lots of medical research physicists that the quality of medical physics research presented at many conferences and scientific articles is degrading, in spite of the fact that it is difficult to provide accurate data therethrough. Major scientific journals, *Physics in Medicine and Biology* and *Medical Physics*, fare very well, but this may be an indicator that the last impact factor (ISI) for medical physics in 2009 decreased significantly for the first time by 30%.

One of the biggest problems is the inconsistency between the current educational structure of medical physicists and the typical role that medical physicists perform. According to a poll by the American Association of Physicists in Medicine (AAPM), most medical physicists currently hold doctorates (Ph.D.). While a Ph.D. is required to conduct the research, it is clear from the previous discussion that most medical physicists are not involved in research, at least not in the research at a level that would lead to scientific publications or research grants. This situation means that we are currently experiencing an excess of qualified and over-trained medical physicists with poor prospects for the future that will naturally lead to the balance, especially in radiation oncology, requiring fewer candidates of science.

The technological orientation of clinical medical physics is reflected in the fact that more and more services traditionally performed by medical physicists are transferred to other professionals (e.g. dosimetricians, technologists) or even companies for outsourcing. Though medical physicists are sometimes reluctant to admit that their level of education and experience may be too high, hospital management is increasingly aware of this when less qualified (and less expensive) specialists are hired instead of the medical physicists. This tendency is expected to continue.

Radiation protection of patients

Medical physicists have another responsibility: radiation protection of the patients. Although the staff protection policies have been long-existing, patients protecting from accidental and unintended exposure is extremely important as well. Radiation therapy is a safe procedure as a rule, but given public concerns about radiation exposure, even minor accidents with minor injuries are the focus of attention in the media. For this reason, the European Union (EU) has consolidated the existing legal framework and adopted a new directive on basic safety standards, which obliges all the EU member states to implement rules to prevent unintentional exposure of patients and assess the risks. The new British Standard Specifications (BSS) apply the role of medical physicists directly. These standards specifically call for the active participation of these professionals in the process; and physicists are considered indispensable for the situations that could put staff or patients at risk preventing and correcting that. It is interesting that in some countries the rules do not require the Radiation Protection Officer (RPO) to be a medical physicist or even that the RPO has a college degree.

Medical physicists should also perform a leading role in assessing evolving problems related to the quality and safety of radiation therapy. They should be involved in clinical trials and risk assessments. Education performs a crucial role in medical physics. Physicists require the appropriate and consistent education before they enter the Faculty of Medicine of Physics, and thereafter, both postgraduate education and ongoing education are required throughout the life.

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DISCUSSIONS

In consideration of the expected rise in cancer morbidity in these countries over the coming years, the key role of medical physicists is crucial and new generations of leaders must be able to combine innovation, efficiency, and co-use for the development of the best possible health for all in one.

CONCLUSIONS

Despite the fact that medical physics is well accepted in the medical field, it is still amazing how much it has to compete for the recognition in the field of physics and continue to prove that it is the 'real' physics. Probably, this is due to the fact that the majority of 'real' physicists primarily see the clinical part of medical physics, where the focus is not on research, but likely on clinical practice. The problem could also be in that medical physics never cared about promoting itself fundamentally, that is, in physics departments, as it was busy seeking acceptance in the medical community. Since medical physics is essentially interdisciplinary and is found between the physics and the medicine, it is no surprise that it has found its place in the medical departments. However, remarkably, it is much more often used in medical faculties than in physical ones. We do not see this as a good long-term survival strategy. We believe that medical physics can become one of the most thrilling, challenging, and usable disciplines of clinical and academic physics, and that it should be advanced as such.

Medicine in general is influenced not only by physics but also by biology and other fundamental sciences. Someone might object that this could lead to a decrease in the relative importance of physics, although the absolute contribution remains at the same level. Nevertheless, medical physicists should cover other disciplines as well as new fields besides radiation oncology and radiology. You may find it a challenging task without reducting of primary (i. e. physical) training and knowledge. However, though curriculum intensification in non-standard subjects may not be appropriate for most medical physicists, those who are 'advanced' should definitely invest the extra time and effort in interdisciplinary teaching that goes beyond typical medical physics.

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