Grand challenges for medical physics in radiation oncology

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Review Article

Grand challenges for medical physics in radiation oncology

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ABSTRACT

Medical physics has made considerable contributions to recent advances in radiation oncology. Medical physicists are key players in the clinical and scientific radiation oncology context due to their unique skill sets, flexibility, clinical involvement and intrinsic translational character. The continuing development and widespread adoption of “high-tech” radiotherapy has led to an increased need for medical physics involvement. More recently, our field is rapidly changing towards an era of “precision oncology”. These changes have opened new challenges for the definition of the professional and scientific roles and responsibilities of medical physicists. In this paper, we have identified four grand challenges of medical physics in radiation oncology: (1) improving target volume definition, (2) adoption of artificial intelligence and automation, (3) development of predictive models of biological effects for precision medicine, and (4) need for leadership. New visions and suggestions to orientate medical physics to successfully face these new challenges are summarized. We foresee that the scientific and professional challenges of our times are pushing medical physicists to accelerate toward multidisciplinary. Medical physicists are expected to innovatively drive interactions and collaborations with other specialists outside radiation oncology while the radiation physics core will remain central. Medical physicists will retain strong and pivotal roles in quality, safety and in managing ever more complex technologies. The new challenges will require medical physicists to continuously update skills and innovate education, adapt curricula to include new fields, reinforce multi-disciplinary attitude and spirit of innovation. These challenges require visionary and open leadership, which is able to merge established roles with the exciting new fields where medical physics should increasingly contribute.

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Radiation medicine started with the discovery of X-rays and radioactivity at the end of the 19th century, leading to diagnostic and therapeutic applications of radiation. Several Nobel prizes in physics and chemistry are part of the history of medical physics in imaging and therapy, with Wilhelm Röntgen and Marie Curie considered by many as the “founders” of the applications of physics to medicine.

More recently, Nobel prizes also in medicine have been awarded to physicists for their achievements, such as the discoveries concerning the molecular structure of DNA, the development of computer assisted tomography (CT), or discoveries concerning magnetic resonance imaging (MRI). In radiation oncology,

physicists were involved from the pioneering applications at the end of the 19th Century, and by 1912–1913 the first physicists were appointed to hospital positions (in Munich and London) [1]. Also academic positions for medical physics appeared early, e.g. Sidney Russ as the first chair in physics appointed at the London medical school in 1920, or Rolf Sievert being appointed as a full professor of medical physics in 1941 in Stockholm.

Ever since, medical physicists¹ have contributed to the technological and clinical advances of radiotherapy and constitute a key profession with a central role within the multidisciplinary approach of oncological care [2,3]. Today, medical physicists are responsible (with other professionals) for guaranteeing a safe and optimal use

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¹ In the context of this contribution, a medical physicist is defined as a physicist employed in hospitals or medical research institutions, being in charge of medical applications of radiation, imaging, as well as radiation protection

of technology in medicine; their flexibility, clinical involvement, intrinsic multi-disciplinary character and unique skills are well recognized and valued both scientifically and clinically, in particular in radiation oncology. Another pivotal point relates to the diverse “job profiles” in medical physics, covering clinical service, academia and research, clinical development and implementation as well as research and development in industry. This diversity is of great value to the medical field and to radiation oncology in particular.

The continuing development and widespread adoption of “high-tech” radiotherapy in recent decades have led to the increased involvement of medical physicists [2–4]. More recently, radiation oncology is changing following the current evolution towards the “precision oncology” era [5]. These developments opened a debate in the radiation oncology physics community regarding the redefinition of medical physics roles and responsibilities in these new scenarios [2,6].

The ESTRO Budapest vision meeting

This paper was prepared by members of a task group on the “Future of Medical Physicists in Radiation Oncology”, created by the ESTRO physics committee. In collaboration with the AAPM working group on Future of Medical Physics Research and Academic Training (FUTURE), it organized a think tank meeting on “the most provocative questions for medical physicists in Radiation Oncology” that was held in Budapest in October 2019. This workshop involved not only medical physicists but also other in-field and out-of-field experts, acknowledged at the end of this paper.

A summary of the major organizational issues can be found in the [Supplementary material](#), including the process to select the four “most provocative questions” that were here identified as the “grand challenges”, with a 10-year horizon. [Fig. 1a–d](#) summarizes in word clouds the discussions referred to the four debated challenges.

Inspired by the lively discussions held in this workshop, the scope of this paper was to present visions and suggestions of the task group, aiming to identify priorities for the future grand challenges for medical physics in radiation oncology.

Target definition transformed from an art to science

Despite the availability of better and better imaging information and the continuously improving knowledge of tumor spread, clinical target volume (CTV) delineation continues to be affected by large inter- and intra-observer variability [7,8]. In other words, delineating the CTV can be still considered as an art, expertly performed by clinicians, according to its literal meaning, intended as a “skill acquired by experience, study, or observation” (<https://www.merriam-webster.com/dictionary/art>). There is therefore considerable room for reducing the uncertainties in CTV delineation through a scientifically-based approach driven by medical physicists. Some evidence suggests that patients are over-treated by the use of too wide CTV margins [9]. For instance, the inclusion of loco-regional lymph nodes in the CTV for elective nodal irradiation often comes with a many-fold volume increase [12], with a negative impact on the surrounding healthy tissues and unclear benefit for survival for some tumor sites such as breast and prostate [13,14]. A few studies looking into reducing CTV margins showed promising results but suffered from large statistical uncertainties [10,11].

Despite the considerable recent advances in imaging, microscopic extensions of the GTV will remain invisible since even advanced imaging techniques are still unlikely to reach the

spatial resolution required to detect a few or single cells. Similarly, lymphatic spread may remain invisible and uncertain. Moreover, the interplay of different treatment modalities, which is becoming the standard of care for some tumor sites, is not well understood. Systemic therapy can take care of microscopic disease and may reduce the need for CTV expansions [15]. The role of the CTV needs to be re-defined, for instance when synergistic effects between radiation and immunotherapy are being considered [16]. Physicists can help to address these substantial challenges from a number of angles:

- 1) It is of primary relevance to collect and combine data such as advanced functional imaging and other biomarker data to enable better characterization of tumor spread characteristics, including lymphatic spread and tumor/host interactions. It has been shown how macroscopic MR imaging can provide microscopic tissue characteristics [17–21]. It will be important to also include longitudinal data, i.e. changes over time. Physicists, among others, have to make sure that the data are FAIR (findable, accessible, interoperable, and reusable). When data are not available, physicists should be involved in collecting new data through clinical trials that are designed similar to physics experiments and can challenge clinical practice, for example by substantially reducing CTV margins.
- 2) Medical physicists, in collaboration with biologists and biophysicists, should explore models for tumor spread pathways [22] as well as the effect of combined treatments on microscopic disease spread, such as radiation-immunotherapy interplay [23].
- 3) Moving toward the development of a framework for probabilistic definition of the CTV is of paramount importance [24,25]. The standard binary (tumor/no tumor) definition does not capture the underlying probabilistic nature of the problem. A probabilistic approach to CTV definition requires the integration of data from imaging biomarkers (e.g., radiomics), patterns of recurrence, pathology data, data from clinical trial with shrinking volume and tumor likelihood map, in order to quantify the risk of marginal recurrence and balance competing risks.
- 4) Initial steps forward would be to implement the most recent CTV consensus guidelines and e.g. to expand the GTV automatically while respecting anatomic barriers to tumor spread [26]. The approaches should be developed for and could be tested in specific disease sites such as head-and-neck, lung and central nervous system.

Development and implementation of artificial intelligence in radiation oncology

Artificial Intelligence (AI) based solutions are currently entering our field for a number of applications [27,28], expecting to impact at professional, health system and patient level, including better access to treatment [29,30]. These solutions need to follow the same technology adoption process as other engineering principles applied in medicine [31]. First, a clinical unmet need or a problem is identified and defined where novel solutions are suggested based on the proposed requirements; next, a validation phase follows to test if the new solutions meet the requirements for use in clinical practice; before finally facilitating end users (e.g. clinicians, radiation therapists, medical physicists) by understanding the principles of AI, crucial for successful and safe implementation in clinical practice [32]. The following four key points are seen as major priorities for medical physics in this area:

Fig. 1. The four grand challenges were debated within the think tank ESTRO meeting on “the most provocative questions for medical physicists in Radiation Oncology” that was held in Budapest in October 2019; the inspiring and lively discussions were considered as a basis for current paper. For each challenge, word clouds based on the recording of the sessions were generated: (a) target definition transformed from an art to science; (b) development and implementation of artificial intelligence in Radiation Oncology; (c) modeling biological effects in the era of personalized Radiation Oncology; (d) leadership in the changing world of Radiation Oncology.

- 1) Implementation and customization of AI technology. The long tradition of successful implementation of new technology mainly comes from the collaboration between medical physicists and physicians, nurses and technologists. This environment places medical physicists in a unique position to contribute to the implementation of AI in the clinical environment together with the AI specialists [27,33]. Therefore, medical physicists should now widen their collaborative space and work together with data scientists and engineering specialists to introduce AI safely and efficiently into the current care path of patients. This starts with an understanding of the technology presently at hand. Although many medical physicists have, by training, strong analytical skills for problem solving [34–37], detailed knowledge about current machine learning, deep learning or other AI techniques is not ubiquitous [32].
- 2) Development of AI technology. Playing the central active role in the upcoming AI field is attractive for physicists who contribute to the definition of the directions that should be taken to secure proper clinical implementation. Collaboration with industry and scientific computing research groups is therefore of utmost importance to have access to the latest technology and scientific insights. A simplistic approach could be to team up with data science/-data engineers to implement already available tools. However, application and interpretation need to come from the medical physics field itself. The success of AI approaches does not only depend on the quality and amount of data needed for training but also on the ability to rephrase the clinical questions towards the data science engineers. Again, collaboration with other disciplines is a key factor for success.

- 3) Facilitating access to proper data. AI typically needs to deal with having access to data [38–40]. The hospital IT environment landscape is changing rapidly and medical physicists should play an active role in this to guarantee access to data sources for AI development. Besides advice on the requirements for the IT frameworks, medical physicists together with the physicians are responsible for interpreting and developing the appropriate models: e.g. prediction models [41,42] or more advanced solutions [43–45]. Technology for data mining is only a single aspect of this work, as challenges are also present in aligning the different stakeholders (IT, physician, legal/patient privacy etc), to strive for collaboration and keeping the common (clinical) goal. Also besides quantity, the quality (e.g. richness, size and amount of curation) of the datasets is of utmost importance for successful training and implementation of AI models in clinical practice.
- 4) Education and training for AI skills. Besides implementation, discussion and interaction is also needed with industry to roll out these new technologies with the innovators and early adopters; however, these partners are currently only a limited fraction of medical physicists, typically located in the larger academic hospitals. Medical physicists dedicated to clinical activities need training for these new developments and programs for commissioning and quality assurance need to be developed. Basic knowledge of AI in the curricula for medical physicists must be secured [46]. The extent of training needed will depend on the specific implementations but as AI applications will be classified as medical devices, the medical physicists should also approach these techniques as such with proper testing and validation (QA) programs in place [47]. Hence, understanding AI models is a crucial step towards clinical implementation, otherwise the outcome of AI based models will be accepted without careful assessment of possible flaws or scenarios that are not predicted properly. In addition, medical physicists, once properly trained, are expected to have an essential role to play in ensuring that other members of the team could become more aware of the pros and cons of AI models and tools.

Modeling biological effects in the era of personalized radiation oncology

Medical physics has a long tradition of contributing to modeling biological effects in radiation oncology. High-impact examples are the quantification of dose-volume effects based on clinical data, being relevant in everyday radiotherapy planning and optimization [48,49] as well as the adaptation and use of fractionation models aimed to translate physical doses into biologically equivalent doses for tumors [50]. Actions aiming to maximize the contribution of medical physics to this field are summarized in the following key points:

- 1) Medical physicists have fundamental physics skills to set up mathematical descriptions of biological or clinical problems, combined with ability to simplify complex relationships to the greatest extent. In addition, medical physics training of fundamental mathematical, statistical, biological and clinical aspects allow medical physicists to relatively easy interact with the professionals required for successful interdisciplinary teams to tackle modeling problems. This makes them uniquely positioned to develop models that describe either population trends or individual behavior of cancer and associated therapies. Medical physicists should focus on developing manageable few-parameter models that

robustly capture principal components of the picture and combine heterogeneous information (e.g. dose/volume, clinical, biological, genomic, quantitative imaging. . .) into interpretable and generalizable predictive models [41,51]. Machine learning and AI-based models, derived from data can be useful, but an appropriate level of understanding and extensive validation are needed to give sufficient confidence for clinical use [52].

- 2) Medical physicists have made significant contributions in radiation biology. However, modern radiotherapy is often delivered in combination with chemotherapy, targeted therapy or immunotherapy. Therefore, it is important to acquire sufficient knowledge and to connect with appropriate expertise (e.g. medical oncologists, imaging experts, pathologists, biologists and immunologists) to be able to contribute in modeling new challenging issues related to the new paradigms of radiation oncology in curing and/or preventing metastatic spread [53]. This includes the interaction with the immune system [54], tumor evolution and metastases [55,56], tumor regression [57], lymphocyte irradiation [58] and toxic effects of combined/personalized treatments [59,60]. In order to be able to address these new classes of problems, teaching curricula will need to be revised to include contemporary materials reflecting current state and evolution of radiation oncology.
- 3) Medical physicists should be directly involved in design, execution and interpretation of clinical trials and in pre-clinical experiments. Clinical trials/pre-clinical experiments should target testable hypotheses originating from the models themselves. These can then either prove or disprove the model or provide grounds for additional insights that would enable refinements of the available models [61]. As previously underlined in the context of CTV definition and AI implementation, medical physicists should also act as facilitators of data gathering and data farming, contributing to building and managing advanced data sharing platforms, as well as within new approaches such as umbrella protocols and basket trials [62–64]. Modern teaching curricula should include more materials on clinical trial design and more emphasis should be put on adding training sessions in clinical trial design specifically aimed at medical physicists at national and international meetings.
- 4) In order to maximize the contribution of medical physicists, their education needs to substantially corroborate biology and radiobiological skills to a larger extent than currently captured in our curricula [2,4,6,46]. In addition, medical physicists should acquire a sufficient level of data analytics expertise (e.g., biostatistics, big data, AI) that can constructively contribute to clinical trial design, execution and analyses.

Overall, medical physicists are expected to contribute in a relevant way to the new challenges of personalized radiation oncology in the current, rapidly changing times. To successfully build on the long tradition of modeling normal tissue and tumor response, both proactive and reactive actions must address the new issues. These require fast adaptation towards the multi- and trans-disciplinary nature of radiation oncology. This process is likely to push more and more medical physicists out of their traditional domains, encountering biology-oriented disciplines and clinical, biology and technical experts outside the strict radiotherapy domain. At the same time, the strong roots of medical physicists in the clinical environment remain a remarkable and unique resource in supporting the translation between biological, pre-clinical and clinical applications. In order to respond in the best way to these exciting challenges, medical physicists are required to orientate their

efforts in adapting and increasing their skills and to actively promote new roles and responsibilities.

Leadership in the changing world of radiation oncology

Medical physicists not only guard quality and safety in radiation oncology, but also often take the first, disruptive steps towards change and improvement. Historically, medical physicists have contributed to the major technological developments in radiation oncology. However, technology only serves a purpose if it addresses a clinical need. Technological development “ad infinitum” is not needed, and time and resources should not be wasted [65]. A challenging example concerns the highly unequal distribution of technology within Europe and even within countries/regions (for instance between large academic Institutions and small hospitals); and still more, this is evident in middle and low income countries. The roles of national and international networks aimed to better ensure proper and safe implementation of new technology as well as of national and international societies (such as IAEA, ESTRO, ASTRO, EFOMP, AAPM...) in supporting auditing, education and tutoring are of primary importance in this context. The future of radiation oncology will unavoidably require a more equalitarian access to treatment, and this also needs adequate leadership in medical physics, including challenging actions toward middle and low income countries. The future will also be in further personalization of the treatment [5,31,51,52,65,66]. This will be achieved through individualized biological based decisions underpinned by robust models. These models will be developed through deep learning and data mining for which the standardization and creative development would benefit of the contribution of medical physicists [67]. Within this scenario, some major key points may be underlined:

- 1) Medical physicists should develop a mutually synergistic partnership with the other professionals in radiation oncology in leading our field together. Here we can consider the analogy of the airplane. The pilots and crew in the plane work together and from time to time one or other is in charge of different aspects of the ‘flight’. This ensures both the fleet and the passengers arrive safely and effectively at the common destination, by the most appropriate means for the scenario. The professions in radiation oncology have different training, which give them different skills. Radiation Oncology needs all of these different types of skills to effectively move the field forward safely and therefore the leadership needed to achieve this must be multi-faceted. The key lies in choosing the right areas for each to lead in, and hence the changing world of radiation oncology will also need medical physicists to be leaders.
- 2) The advancement of any field needs *episteme* (know what, concepts and logic), *techne* (know-how, inter-disciplinary) and *phronesis* (know what, when and for whom, researchers, practitioners etc). To achieve this in radiation oncology we need both an artistic and scientific approach. Medicine for the individual requires the art to be underpinned by the strongest science, which is where physics plays a crucial role, in identifying and developing new scientific concepts that can support radiation oncology developments.
- 3) To continue to be leaders, the responsibility lies with the medical physicists themselves. The majority of clinical medical physicists work in hospitals, delivering radiation oncology to the best of their ability and in some cases leaving little time for innovative thinking [6]. This may cause frustration in medical physics teams, therefore it is crucial to have the right leaders in the right position with the right education

and training and networks to drive innovation. Not secondarily, educating outsiders (policy makers, managers) and the public regarding the essential role of medical physicists is also relevant [46,68].

- 4) The fact that radiation oncology has worked so well in the past is because medical physicists were part of the team. The role for Medical physicists should be to horizon scan to identify relevant scientific and technological advancements that may have relevance to radiation oncology such as the role of wearable devices or flexible printable detectors, as only two examples. This then naturally leads to leadership of all technological innovations (in both soft and hard technologies) that will be introduced in the hospital, where the medical physicists will play a central role guiding the clinical engineers, data scientists and biomedical engineers in asking the right questions. Medical physicists will continue to lead in facilitation of implementation of technology, including new directions such as AI, as discussed in a previous section, and ensuring explainability and impact for patients [65]. This has a wider reach in the hospital beyond radiation oncology, radiology and nuclear medicine departments. Therefore, for optimal effective leadership, medical physics departments should have some autonomy to not only be focused on radiation oncology, such that they are able employ a greater variety of scientists, as has been seen in imaging departments. In this way, both radiation oncology and other medical disciplines would benefit from the inter-disciplinarity across the whole field of medical physics.

Visions for grand challenges: concluding remarks

Table 1 summarizes key bullet points (with a 10-year horizon) for the four major grand challenges. Importantly, although identified under the angle of medical physics, they may be, at least in part, of interest to the whole radiation oncology community. New visionary roads are needed to optimally address the grand challenges of our times and of the coming future. A common message, largely present in all four challenges, is that the field of medical physics should accelerate toward multidisciplinary [3,4,69–71], with different problems and unexplored fields to be explored. This is connected with the intrinsic translational nature of medical physics but also contains something new, mostly linked to the rapid evolution toward personalized medicine, stressing the growing need of hybridization. Medical physics in radiation oncology has to extend its interest beyond the core of radiation physics such as high-tech expertise, quality assurance and radiation safety. Medical physicists are expected to courageously move away from the “radiation oncology exclusivity”, increasing and activating interactions and collaborations with other specialists such as engineers, statisticians, biologists, mathematicians, biophysicists, data scientists, imaging scientists as well as physicians outside radiation oncology including radiologists, medical oncologists, immunologists, pathologists and surgeons. This evolution can be considered perfectly in line with the attitude of medical physicists to work as part of a team and with the intrinsic multi-disciplinary nature of radiation oncology; in other words, with the traditional ability of medical physics to adapt its roles to new and disruptive challenges to the progress of radiation oncology.

A relevant issue concerns the limited availability of resources to make these processes faster, through an adequate support in terms of dedicated time and man-power. The complexity of this point is out of the aims of current work; however, we may expect that extending the interests toward the “new fields” could facilitate the access to grants and funds that can better attract talented young physicists as well as create more opportunities for dedicated

Table 1

Challenges	Key words	Bullet points
<i>Target definition transformed from an art to science</i>	image-based tumor characterization, data collection, clinical trials, tumor spread, probabilistic targets, guidelines implementation	<ol style="list-style-type: none"> 1) MPs should collect and combine biological and imaging data, enabling better characterization of tumor spread characteristics. 2) MPs should model the effect of combined treatments on tumor spread pathway. 3) MPs should develop a framework for probabilistic definition of CTV to quantify the risk of marginal recurrence and balance competing risks. 4) Existing clinical guidelines should be implemented as algorithms in treatment planning systems
<i>Development and implementation of AI in RO</i>	AI implementation, customizing AI solutions, data access, translating clinical requests, AI-oriented education and training	<ol style="list-style-type: none"> 1) MPs are in a unique position to drive implementation and customization of AI technology in RO, in collaboration with vendors of AI solutions. 2) MPs are expected to contribute in specific AI developments, mostly in teams including other specialists, such as engineers and data scientists. 3) MPs will have a pivotal role in facilitating the access to the proper data, needed for efficient and successful AI solutions and in striving collaboration between different professions and sciences. 4) Most clinical MPs will not be involved in developing AI solutions but will consider them as additional medical devices; then, specific AI-oriented education and training have to be set in the core curricula
<i>Modeling biological effects in the era of personalized RO</i>	interpretable models, combined treatments, immunology and immunotherapy, clinical trials, curriculum in biology	<ol style="list-style-type: none"> 1) MPs have unique skills to set up simplistic, yet realistic biological models. 2) Models should expand beyond RO to capture modern multi-modal treatments. 3) MPs should be involved in clinical trials and experimental designs to capture relevant modeling parameters. 4) MPs should reach out of the traditional RO domain with updated curricula.
<i>Leadership in the changing world of RO</i>	synergy, high scientific profile, multi-disciplinarity, innovation, education, leadership selection	<ol style="list-style-type: none"> 1) Synergy is needed between other RO professionals and MPs to lead the field together: the leadership needed to achieve the best for the field must be composed from all 2) RO for the individual has both an “artistic” and scientific approach where “art” must be underpinned by the strongest science 3) The responsibility for leadership lies with the MPs themselves to have the right leaders and the right education to drive innovation. 4) The future of MP lies in MPs leading a multidisciplinary team of other engineers and scientists.

MP: medical physics, MPs: medical physicists; RO: radiation oncology; ROs: radiation oncologists; AI: artificial intelligence.

resources to innovation and research for medical physics departments. Also due to this context, structured medical physics departments incorporating both clinical and scientific/research roles will also be pivotal in successfully facing these challenges [2,4,6]. If possible, the integration of different non-medical professionals within large and structured medical physics departments may represent a relevant additional value for radiation oncology.

This changing scenario will pose challenges concerning the preparation and selection of a new generation of visionary leaders. The radiation physics core will remain an important part of both clinical and scientific work in medical physics in radiation oncology, including the strong and pivotal role in managing quality, safety and ever more complex technology. In Europe there is a legal framework (EC directive) with varying national interpretations, which describes the role of the medical physics expert (MPE) and this cannot be ignored [72]. On the contrary, this has to be considered as a well assessed and strong base for medical physicists, primarily contributing to its strength in the clinical environment, with pivotal roles in assuring quality and safety, and even to its unique position in facing the new challenges. It is likely that the new challenges will rapidly translate into new roles and responsibilities that should gradually integrate and extend the current legal framework for the MPE in radiation oncology. New requests mean new (multi-disciplinary) fields to be explored, and this means the need for continuously updating skills and education, adapting our core curricula [46]. This point is likely to be one of the most challenging, due to the heterogeneous situations in the different European countries and to the intrinsically slow reactivity of the education systems. The multi-disciplinary nature of ESTRO and its flexibility can greatly contribute to accelerating and supporting these processes [6]. A shared leadership between the different

disciplines within ESTRO, with particular emphasis on medical physics, would be beneficial. For better engagement with other fields of medical physics and the ability to integrate the best of them into radiation oncology, actions to reinforce and intensify relationships with other international medical physics societies are of high relevance and importance.

Finally, the need for action to facilitate efficient and equal distribution of technology in middle and low-income countries is an urgent and highly challenging issue of our times. Given the expected increase in cancer in these countries in the coming years [73–75], the pivotal role of medical physicists is crucial and new generations of leaders must be able to merge innovation, efficiency and sharing to create optimal health for all, together [76].

Conflicts of interest

No conflicts of interest to declare.

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Appendix A. Supplementary data

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