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Original paper

The role of medical physicists in clinical trials across Europe

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ABSTRACT

Introduction: The roles and responsibilities of medical physicists (MPs) are growing together with the evolving science and technology. The complexity of today's clinical trials requires the skills and knowledge of MPs for their safe and efficient implementation. However, it is unclear to what extent the skillsets offered by MPs are being exploited in clinical trials across Europe.

Methods: The EFOMP Working Group on the role of Medical Physics Experts in Clinical Trials has designed a survey that targeted all 36 current National Member Organisations, receiving a response from 31 countries. The survey included both quantitative and qualitative queries regarding the involvement of MPs in trial design, setup, and coordination, either as trial team members or principal investigators.

Results: The extent of MPs involvement in clinical trials greatly varies across European countries.

The results showed disparities between the roles played by MPs in trial design, conduct or data processing. Similarly, differences among the 31 European countries that responded to the survey were found regarding the existence of national bodies responsible for trials or the available training offered to MPs. The role of principal investigator or co-investigator was reported by 12 countries (39%), a sign of efficient collaboration with medical doctors in designing and implementing clinical studies.

Conclusion: Organisation of specific training courses and guideline development for clinical trial design and conduct would encourage the involvement of a larger number of MPs in all stages of trials across Europe, leading to a better standardisation of clinical practice.

1. Introduction

Medical physicists (MPs) play a key role in clinical science, including assuring the safe and effective use of radiation for diagnostic and therapeutic purposes [1–4]. Many advances in radiology and radiotherapy have been driven by MPs. Modern medicine - including cancer treatment – would look very different without the existence of medical physics as a profession. Consequently, nearly all clinical trials will

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involve one or more technologies, be they diagnostic or interventional, which are reliant on the skills and expertise of MPs for their use.

Given the ever-increasing complexity of clinical trials and the costs involved, harmonization remains a major role of trial design and conduct. This includes the strong need to ensure reliability and reproducibility in the acquisition of diagnostic and prognostic imaging, especially with an increasingly broad range of imaging biomarkers that may be structural/morphological, textural, or functional. Thus, many endeavours have been made to provide general imaging modality harmonization from an image acquisition perspective across multicentre studies [5–7]. This includes specific clinical indications such as brain diffusion MRI [8], general neurological MRI [9], PET oncology trials [10,11] and lung CT [12] to name but a few. In the therapeutic setting, it is well-established that quality assurance (QA) in clinical trials results in more reliable trial results and most likely directly affects patient outcomes [13–18]. This has been documented for external beam radiotherapy in particular, but standardisation of e.g. radionuclide therapy administrations is also key to establish dependable dose–effect correlations, the quality of which can impact treatment efficacy [19,20]. Standardisation of imaging and treatment between departments and countries may furthermore have wider impact [21,22], thus also benefitting patients treated outside of trials [23]. Such QA efforts will most commonly fall to MPs to define, design and implement [24–26].

However, the potential role of MPs in clinical trials can extend well beyond QA [27]. Providing the link between technical expertise and clinical knowledge, MPs are uniquely placed to suggest how technological advancements may offer improved patient outcomes and how they can be leveraged for the benefit and optimization of clinical trial design and endpoint generation. With many MPs involved in research and development, often in part- or fulltime academic roles, they provide a clear link to evolving technologies. Additionally, given the strong quantitative, systematic and analytical propensity, and training in data visualisation and interpretation of evidence, MPs can help multiply the knowledge gained from trials [28–31].

Involving MPs in the design and conduct of trials should thus be of interest to all. In this context, the AAPM Task Group 113 published a guidance document on the Physics Aspects of Clinical Trials [25], but these comprehensive guidelines do not cover the specificities of the role of MPs in Europe. Furthermore, it is currently unclear to what extent the unique skillsets provided by MPs for clinical trials are being utilised across Europe. With this in mind, the EFOMP Working Group (WG) on the role of Medical Physics Experts in Clinical Trials set out to gather information on the current roles and responsibilities played by MPs in clinical trials across all specialties in EFOMP National Member Organisations (NMOs) across Europe.

2. Methods

The working group designed a survey that targeted all NMOs within EFOMP. The questionnaire was sent out in May 2021 to all 36 current NMO members of EFOMP. Results of the questionnaire were collected between May 2021 and October 2021. The questionnaire was directed to NMO Presidents and EFOMP delegates. Answers were collected through the Google Forms platform, an open-source web-based application for surveys. The questionnaire can be found in the appendix.

The 20 questions of the survey included both quantitative and qualitative (open ended) queries regarding the involvement of MPs in trial design, setup, and coordination, either as trial team members or principal investigators. The survey was developed by the 15 subgroups of the WG, each with a specific focus point across MP roles in clinical trials, ensuring all potential topics were addressed. The draft version of the survey was checked among the WG and tested on a couple of external test subjects.

3. Results

Of the 36 NMOs which are part of EFOMP, 31 responded to the survey (86%). Based on the answers provided, in most countries the majority of trials with medical physics involvement are initiated by individual academic investigators or centres, followed by national clinical / academic organisations within the respective country or from other countries. Industry-initiated trials are not as common as those inducted by non-industry organisations, such as EORTC (Fig. 1).

Most EFOMP NMO countries do not have a national central body for running clinical trials (74%) nor a body responsible for coordinating clinical trial quality assurance (71%) (Fig. 2). Of those countries that have a national structure for coordinating clinical trials, most responded positively regarding the existence of legal requirements or established pipelines for MPs to be involved in conducting a clinical trial. Very few countries (2 countries, 7%) have published guidelines in this respect. However, 11 NMOs (36%) confirmed that MPs are part of Institutional Review Boards or Independent Ethics Committees involved in clinical trial setup and coordination (Fig. 3). The input of MPs in these bodies is mainly required for their expertise in medical devices and health technologies, or for other technical assistance. It is possible for MPs involved in clinical trials to take up the role of principal investigator or co-investigator in a similar proportion of countries (12 countries, 39%). However, when asked about their awareness of physics-led clinical studies (either as PI or co-PI) in their countries or in international studies, slightly fewer (32%) of NMOs responded positively, while the rest were not aware of clinical trials led by physicists.

Ten countries (32%) reported that for national radiotherapy or nuclear medicine studies, physicists are part of the Trial Management Group (TMG) and / or participate in the writing committee of clinical trials (Fig. 4). In 39% of NMOs MPEs are members of national clinical studies or multidisciplinary disease groups, led by national foundations, oncology societies or working groups initiated to design clinical trials on a specific topic. The same percentage of NMOs (39%) reported that in their country MPs are not invited to join national clinical groups in charge of guideline developments for clinical trials, whereas the remaining respondents could not confirm or infirm the involvement of the MPs in such committees.

Medical physicists involved in clinical trials (whether national or international) reported to have multiple roles throughout all phases of the trial – from design to quality assurance and data analysis (Fig. 5). While most duties are related to radiation protection for patients and staff (58%), radiotherapy QA and credentialing for imaging and therapeutics (52%), there are several other aspects MPs bring their contribution to. Dummy runs to support intervention and development of outlining guidelines are also often reported as part of MP's roles (42%). Participation in data collection is not uncommon either, with 29% of respondents listing this item as a normal role for MPs. While secondary data analysis and long-term data management, including data description and access, are less common tasks, about 26% of NMOs stated MPs involvement in primary data processing or complex data analysis such as imaging analysis, dose calculations, the employment of artificial intelligence techniques. Some NMOs mentioned the medical physicists' participation in interim analysis, designation of stopping rules, and power calculations.

Of all NMOs confirming the involvement of MPs in clinical trials only 5 reported implications in nearly all aspects from clinical trial design to complex data processing. Four NMOs reported limited roles (1–2 roles), 8 countries listed between 3 and 5 aspects that MPs contribute with, while 6 NMOs reported 6 to 9 roles that MPs play in clinical trials.

Trial specific QA programmes are most commonly designed by MPs participating in the trial team (32.2%) followed equally by multidisciplinary trial team and the clinical leads (including medical doctors) (19.4%). Local teams (whether physicists or multidisciplinary) are less involved in this task, while the principal investigator was only reported by 12.9% of respondents to be responsible for the trial-related QA

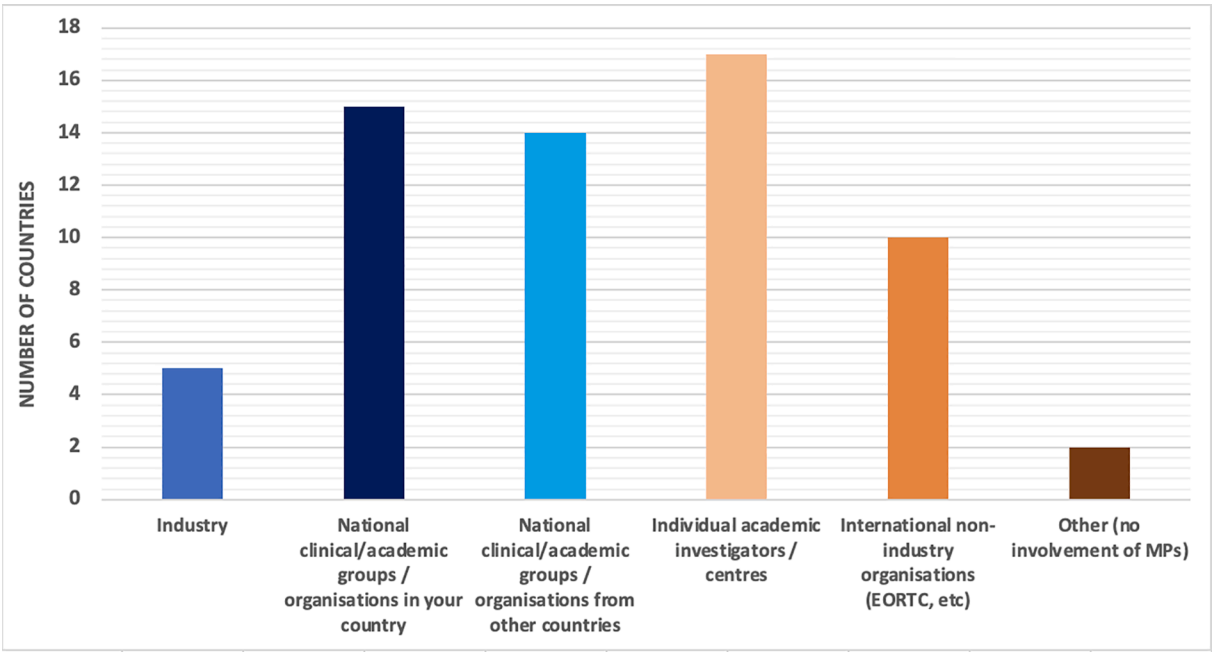

Fig. 1. Distribution of trial-initiating organisations in EFOMP countries (multiple answers were allowed).

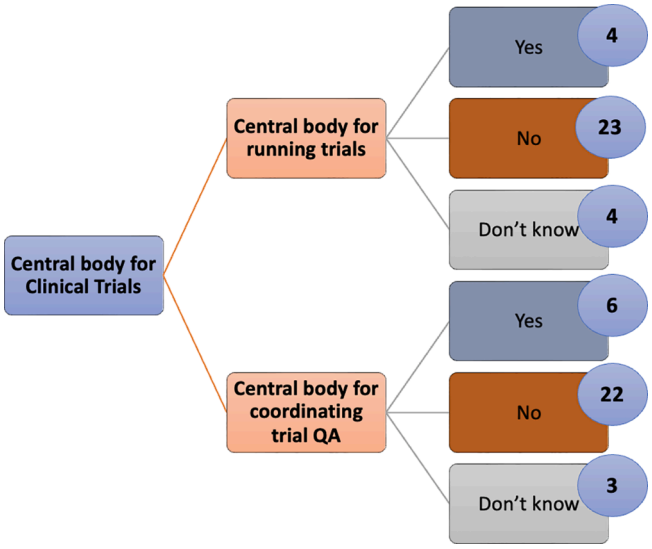

Fig. 2. Status of central bodies for running or coordinating clinical trials in EFOMP countries.

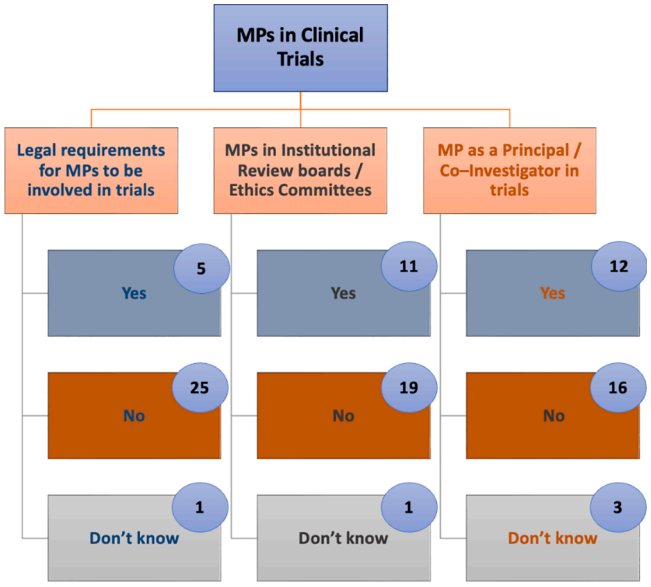

Fig. 3. Involvement of medical physicists in clinical trial setup and coordination across EFOMP countries.

programme (Fig. 6).

Over half of the NMOs participating in the questionnaire (58%) reported that there is no guidance for the level of QA required based on the complexity of a trial, although one member state mentioned that national workshops have been planned but were postponed due to the COVID-19 pandemic. Only 16% NMOs reported the existence of guidance documents (while 26% did not know whether such documents existed). One NMO reported that QA guidance exists but only for clinical trials of drugs.

Credentialing of trials by national dosimetry groups is performed in 29% of NMOs. Of these, equipment is being sent on a national level to all centres involved in two countries, institutes are using their own equipment in another two countries, and one NMO reported that dosimetric measurements are performed by a central dosimetry team. Four respondents are using a combination of the above methods. It was also noted by respondents that in some cases the contribution of national or international laboratories which provide services for clinical trials is being sought. Among the 58% who replied that there are no national dosimetry groups, one NMO stated that the multidisciplinary teams arrange national audits to be performed using Imaging and Radiation Oncology international credentialing services and one NMO reported that they are trying to establish such a group. The rest of the represented NMOs (13%) were not aware of this practice in their countries.

Regarding the existence of RT / imaging data repositories for trial data, 4 out of 31 NMOs stated that they have national repositories for trial data while 20 NMOs (64.5%) responded negatively. While three NMOs reported that local repositories and solutions are in place, seven countries could not confirm or infirm the existence of such trial data repositories.

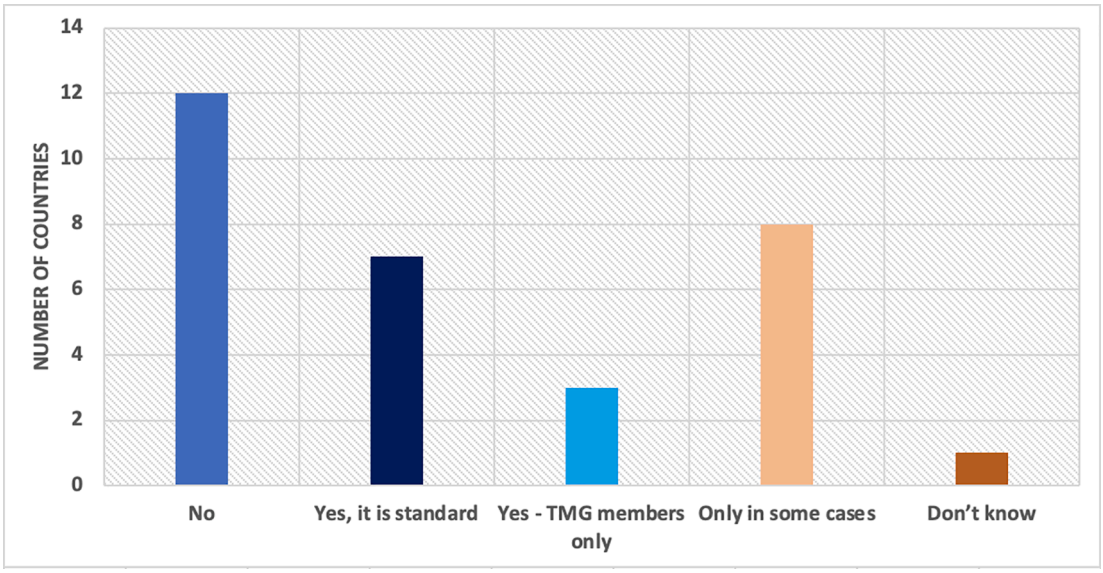

Fig. 4. Status of medical physicist participation in Trial Management Group (TMG) and writing committees of clinical trials across EFOMP countries.

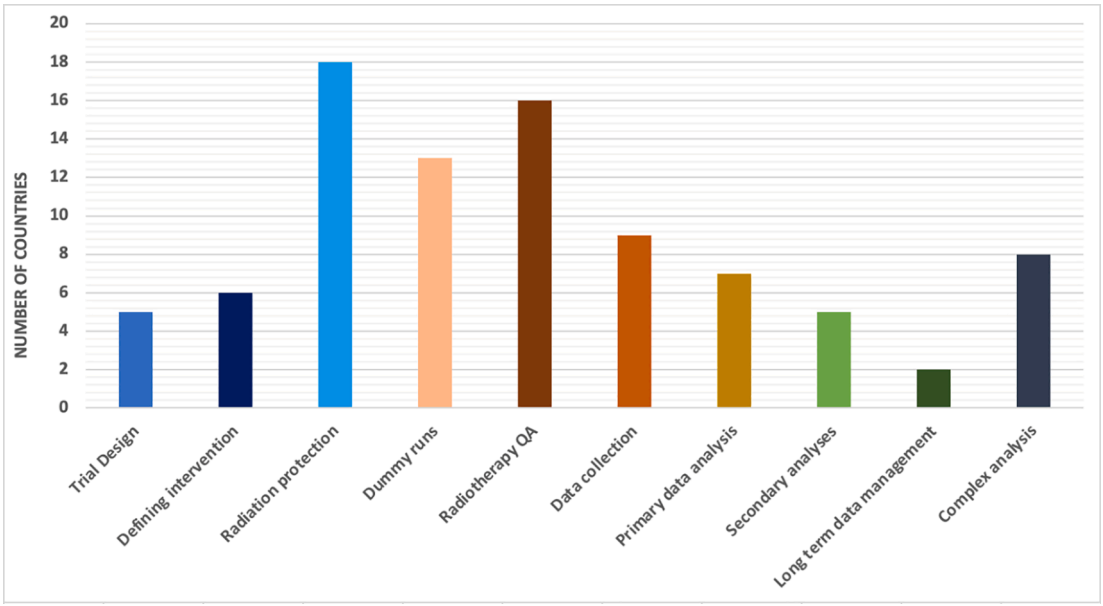

Fig. 5. The role of medical physicists involved in clinical trials across EFOMP countries (multiple answers were allowed).

Dedicated training is available for working in clinical trials in 14 countries (45%). The following best practices were identified: Good Clinical Practice (11 NMOs), Trial design and leadership (2 NMOs) and Regulatory issues (2 NMOs). Only one NMO reported the existence of a dedicated training specific to MPs, whereas in seven countries training is multidisciplinary. One NMO reported regular courses for physicians and MPs and another one stated that training is usually directed to trial nurses in drug-related company trials.

4. Discussion

Clinical trials involve research on human volunteers to bring additional knowledge to the existing medical experience and understanding to prevent, diagnose and treat a specific condition or disease. In cancer research, clinical trials are developed for testing new technologies (whether for medical imaging or therapy), new treatment regimens, new drugs or other novel interventions. Given that MPs play complex roles in many aspects of diagnostic imaging and treatment, involving both ionising and non-ionising radiation, and other devices, their contribution to clinical trials is becoming critical.

Considering the above, a survey was designed by our working group and disseminated to EFOMP NMOs across Europe to understand better the current role played by MPs in clinical trials across the continent. The survey data paint an extremely varied picture. As expected, the clinical responsibilities of MPs within clinical trials are mainly focused on local site credentialing, QA and radiation protection. Approximately one third of European countries MPs also have non-clinical responsibilities, in the form of taking part in Institutional Review Boards (IRB), Independent Ethics Committees (IEC), TMGs or the writing committee, being the principal investigator or co-investigator, and participating in national clinical guideline development groups. Additionally, one fourth of NMOs reported that MPs are involved in complex data analysis and long-term data management. This clearly demonstrates that the multimodality of tasks offered by MPs is recognized in some European

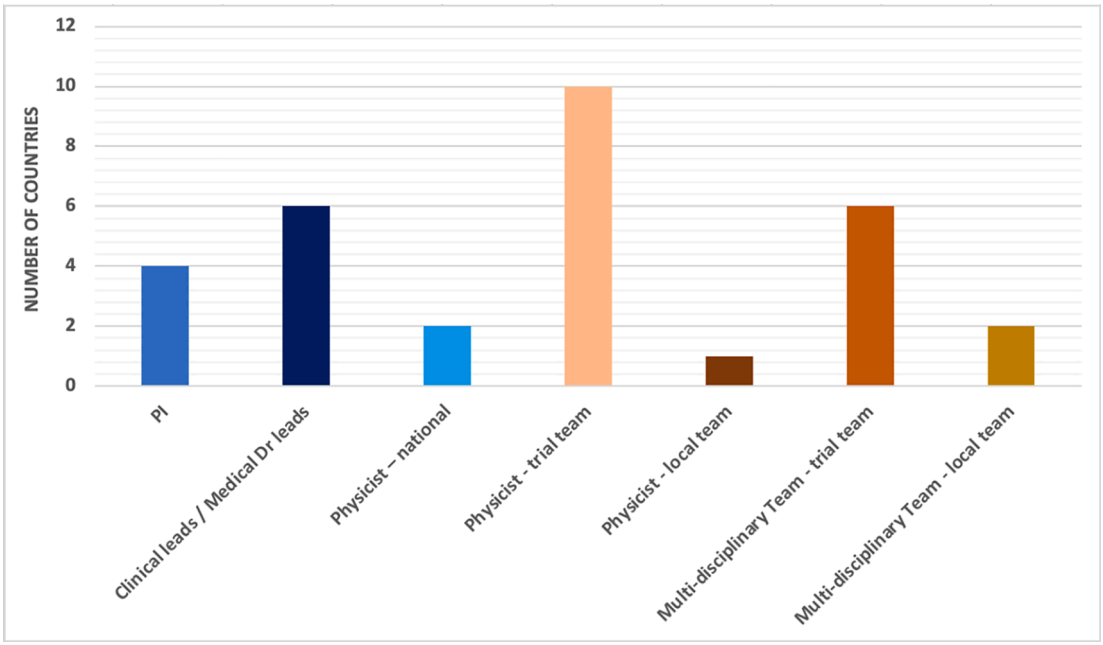

Fig. 6. Responsible party for the design of clinical trial-specific QA programme across EFOMP countries (multiple answers were allowed).

countries, while some others still do not attribute an active (non-clinical) role to MPs within clinical trials.

New technology plays a major role in the advancement of clinical trials and MPs are required to be aware of major technology developments in both imaging and therapeutic settings. This encompasses but is not limited to large axial field-of-view PET [32], photon counting CT [33], organ/tissue specific gamma cameras [34–36], simultaneous multi-contrast MRI [37,38], identification of new biomarkers [39,40], automated treatment planning [41], adaptive RT [42,43], SRS/SRT/SABR [44,45], MRI guided radiotherapy [46], particle therapies [47], flash radiotherapy, new hypofractionated schemes and relevant radiobiology [48]. Additionally, advances in artificial intelligence in almost all clinical phases of imaging and therapy require MPs to have detailed awareness of its routine capabilities and limitations. This also applies to trial QA: recent works have investigated the use of automated QA [49–51], use of which within the context of clinical trials requires close oversight by MPs to ensure adherence to locally set tolerances.

The presence of a national central body for running clinical trials, i.e. under the responsibility of the Ministry of Health or Research, is not common and indeed the results of the questionnaire report that most EFOMP countries do not have a national central body for this task (74%). This is likely a true picture of the current situation given that non-industry related research is mostly conducted by cooperative groups or scientific associations at the national and international level, and not by central government bodies, that in some cases act as a funder of the studies. International collaborations are often intrinsically preferred, in particular in phase 3 clinical trials, because the proposed intervention, being either technology- or pharmacy-related, shall be universally applicable to all patients in different healthcare systems.

Eleven countries confirmed that MPs are involved in IRB/IEC as experts in medical devices and health technologies. Since many clinical trials involve irradiation of trial participants using ionizing radiation, it is ethically important that research ethics committees and individual volunteers understand risks of medical research exposures. The international landscape for medical research dose and risk assessments is based on the Declaration of Helsinki that protects human subjects participating in research, requiring risk/benefit analysis and informed consent. This is clearly stated by EU Directive 59/13 that in its pillar on justification and optimization states that at Art 55, 2 e) that "medical exposure for medical or biomedical research are examined by an ethics committee, set up in accordance with national procedures and/or by the competent authority".

Therefore, it is quite appropriate that MPs contribute to IRB/IEC due their expertise in patient radiation protection, i.e. calculating dose, estimating risks to participants, and, if required, recommending revision of explanations of risk in protocol and participant information sheet.

Regarding the role of MP in clinical practice the questionnaire evidenced MP involvement in clinical trials to take up the role of principal investigator or co-principal investigator in 12 countries (39%). This is clearly a sign of efficient collaboration with medical doctors in designing and implementing clinical studies. This is further testified by noting the participation of MPs in the TMG and writing committees that was reported to be present in 18 countries. Moreover, in 39% of NMOs MPs are members of national clinical studies or multidisciplinary disease groups, led by societies or working groups initiated to design clinical trials.

Our article, which has the typical limitations of survey-based studies [52,53], used results from a pool of answers that present a very high response rate (86%) and can thus be considered representative of the situation concerning MP implementation in clinical trials among the EFOMP NMOs across Europe. Validity of our questionnaire was indirectly checked via the fact that our results suggest that MPs in EFOMP countries are involved in 8% of industry-led trials. A quick search on https://www.clinicaltrials.gov in April 2022 showed 127.896 industry-led trials and a total of 12.053 (9%) amongst them with the terms "Radiology", "Nuclear Medicine" and "Radiation Therapy". Although this 9% could be an overestimation, since some of these trials can be overlapping, the number is in line with our results.

Only two NMOs reported the existence of national guidelines for the contribution of MPs in clinical trials. Additionally, specific training programs for clinical trials have been mentioned to exist in just under half of EFOMP's NMOs. The very heterogenous landscape of actual involvement of MPs in trials may be thus due to both lack of national (and international) guidance as well as the varied access to training, as has been shown elsewhere [54]. Based on our findings, we propose the creation of more training programs on a national level. These initiatives should be endorsed and helped by EFOMP via, for example, Special Interest Groups, or by bringing together (by means of a new Working Group) people who have successfully managed to implement such endeavours within their country with others who are interested in doing so.

To address the lack of guidelines, the EFOMP WG on the role of MPs in Clinical Trials aims to produce a guidance document, demonstrating where MPs can and currently add value to the different stages and activities of a clinical trial. The document will highlight the possible roles and, where feasible, give examples of current institutions. This questionnaire will form the basis of what areas and possible roles the document should focus on to give guidance to MPs across Europe on how to expand their roles in clinical trials if they so wish, with additional aims to increase collaboration and consistency across Europe.

5. Conclusions

This questionnaire aimed to gather information on the current roles and responsibilities medical physicists play in clinical trials across all specialties and all European countries that are members of EFOMP. We have demonstrated the vast array of roles MPs can have in clinical trials and highlighted the wide variety and differences in these roles across EFOMP NMO countries.

The results showed disparities between the national bodies and/or training available for clinical trials across the 31 European countries that took part in the survey. Also, it was emphasized that medical physicists were strongly involved in trial QA and radiation protection, but less in trial design and data collection or analysis. Therefore, it would be of interest to develop training on the role of MP in clinical trials at national and European levels to encourage more involvement of MPs at all stages of trials across Europe. Special editions of the European School of Medical Physics Expert (ESMPE) can be organized in collaboration with the NMOs in order to reach the medical physics community. International guidelines are thus required to offer MPs an adequate framework for all aspects that clinical trials entail.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix

EFOMP survey on the role of medical physicists in clinical trials in Europe

This questionnaire has been developed by the EFOMP Working Group 'The role of the Medical Physics Expert in Clinical Trials'.

The purpose of this questionnaire is to gather information of the current roles and responsibilities medical physicists play in clinical trials across all specialisms and all European countries.

1. Email*
2. Name of National Member Organisation (NMO)
   - Short-answer text
3. Country
   - Short-answer text
4. In your country, would you say that majority of trials with medical physics involvement (however small) are initiated by (multiple answers possible):
   - Industry
   - National clinical/academic groups / organisations in your country
   - National clinical/academic groups / organisations from other countries
   - Individual academic investigators / centres
   - International non-industry organisations (EORTC, etc)
   - Other (text box)
5. Do you have a central body for running clinical trials?
   - Yes
   - No
   - Don't know
   - Other (text box)
6. Are there any central bodies with responsibility for coordinating clinical trial QA?
   - Yes
   - No
   - Don't know
   - Other (text box)
7. Are there legal requirements/established pipelines for medical physicists to be involved in establishing/running a clinical trial?
   - Yes - written / published guidelines
   - Yes – other
   - No
   - Don't know
   - Other (text box)
8. Are medical physicists currently able to sit on Institutional Review Boards / Independent Ethics Committees? If yes, what role do/can they have (please add details)
   - Yes
   - No
   - Other (text box)
9. What role can a medical physicist (legally) play on a clinical trial - can they be PI and/or co-PI?
   - Yes – PI
   - Yes - Co-PI
   - No
   - Other (text box)
10. Are you aware of examples on physics-led clinical studies (as PI or co-PI) from your country?
    - Yes - in my country - provide details
    - Yes - in national and international studies – provide details
    - No
    - Other (text box)
11. Are there medical physicist members of national clinical studies groups / multidisciplinary disease groups?
    - Yes - provide give details
    - No
    - Don't know
    - Other (text box)
12. For national radiotherapy or nuclear imaging studies, do physicists participate in the writing committee or are they Trial Management Group (TMG) members?
    - No
    - Yes, it is standard
    - Yes - writing committee only
    - Yes - TMG members only
    - Only in some cases
    - Other (text box)
13. For physicists on TMG, and/or involved in protocol writing, which of the following roles would they normally take?
    - Trial Design
    - Defining intervention (e.g. treatment details)
    - Radiation protection issues (for personnel)
    - Radiation protection (for patients)
    - Dummy runs (to support intervention & QA development, e.g. to support development of outlining guidelines)
    - Radiotherapy QA (RTQA) - credentialing (imaging & therapeutic)
    - Data collection
    - Primary data analysis / Data processing
    - Secondary analyses

- Long term data management (including data description and access)
- Complex analysis (e.g. imaging analysis, dose calculation, artificial intelligence techniques)
- Other (text box)

14. Who is responsible for designing trial specific QA programmes?
    - PI
    - Clinical leads / Medical Dr leads for the trial
    - Physicist – national
    - Physicist - trial team
    - Physicist - local team
    - Multi-disciplinary Team - trial team
    - Multi-disciplinary Team - local team
    - Other (text box)
15. Is there any guidance in your country for the level of QA required, based on the complexity of trial?
    - Yes
    - No
    - Don't know
    - Other (text box)
16. Credentialing of trials: Are there any national dosimetry groups, and what functions would they perform? (equipment sharing, acquisition protocols etc)
    - Yes - Dosimetry credentialing using institutes own equipment
    - Yes - Dosimetry credentialing using national piece of equipment sent to all centres
    - Yes - Central dosimetry team performs dosimetry measurements
    - No
    - Don't know
    - Other (text box)
17. Does your country have any imaging/RT repositories for trial data?
    - Yes
    - No
    - Don't know
    - Other (text box)
18. Is there any dedicated training available for working in clinical trials?
    - No
    - Yes - specific to Medical physicist
    - Yes - multi-disciplinary
    - Yes – other
    - Regulatory issues
    - Good Clinical Practice (GCP)
    - Trial design & leadership
    - Other (text box)
19. Are you willing/able to share a follow-up questionnaire to any relevant institution/hospital with a medical physics department where clinical trials are performed?
    - Yes
    - No
    - Don't know
    - Other (text box)
20. Please add anything that you feel has not been covered above
    - Long-answer text

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