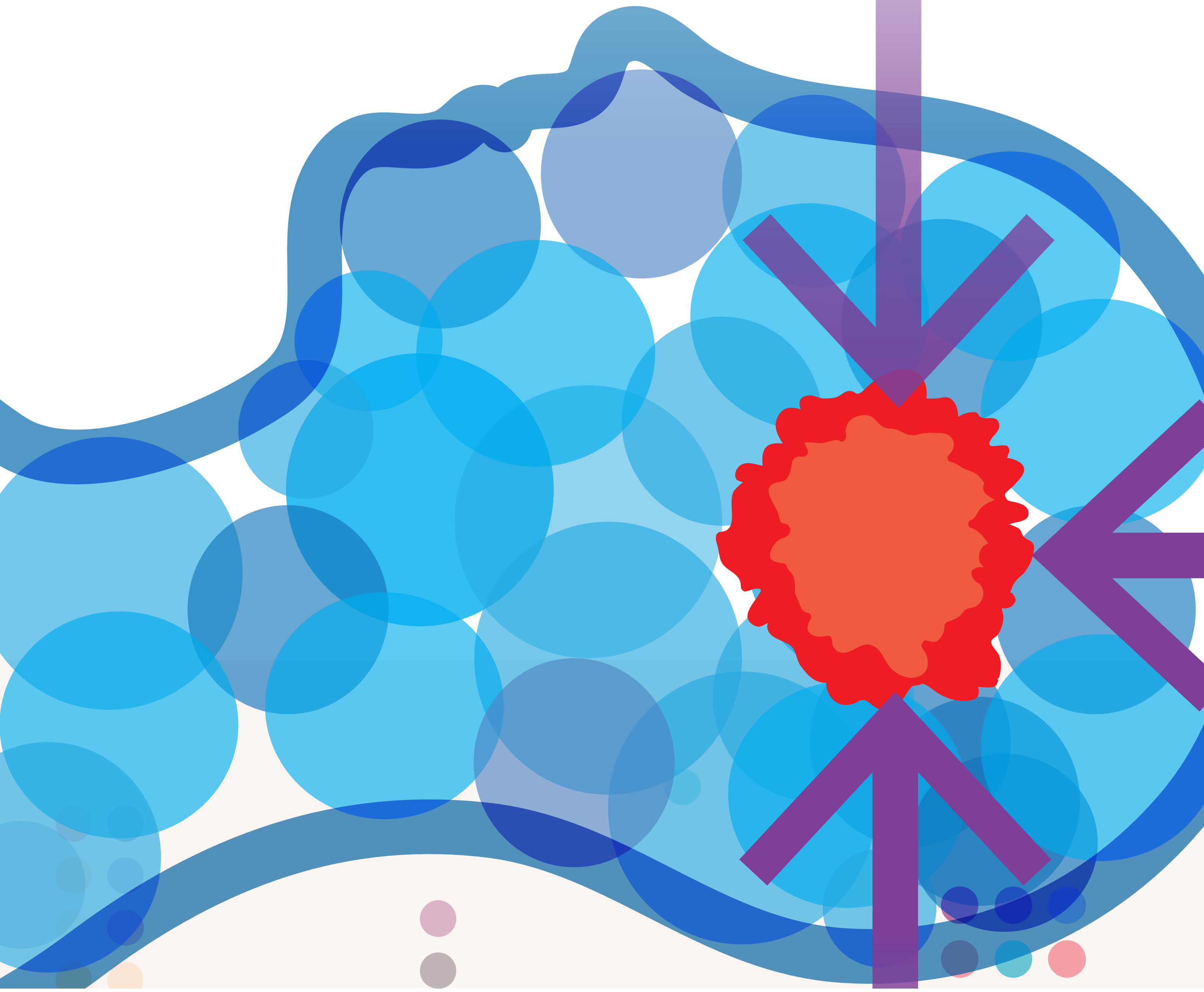
Advances in Radiation Oncology (ICARO-2)

Topical Overview and Conclusions of an International Conference



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ADVANCES IN RADIATION ONCOLOGY (ICARO-2)

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PROCEEDINGS SERIES

ADVANCES IN RADIATION ONCOLOGY (ICARO-2)

TOPICAL OVERVIEW AND CONCLUSIONS OF AN INTERNATIONAL CONFERENCE

INTERNATIONAL ATOMIC ENERGY AGENCY
VIENNA, 2020

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FOREWORD

Cancer claimed an estimated 9.6 million lives in 2018, making it the second leading cause of death worldwide. Left unchecked, an estimated 29.5 million new cases of cancer and 16.3 million cancer related deaths are expected worldwide by 2040. Worldwide, the increasing cancer burden is placing great pressure on healthcare systems and on leaders to provide effective solutions. The countries shouldering the heaviest burden of cancer incidence and mortality possess very limited capacity for dealing with the disease owing to limitations in infrastructure, human resources and access to various components of cancer management.

Radiotherapy has a key role in cancer care, with approximately 50% of all cancer cases requiring its use in treatment. While it is a proven cost effective tool for cancer treatment, access to radiotherapy is still limited in many low and middle income countries. This translates into a global shortage of radiotherapy treatment machines and trained staff.

In 2009, at the request of Member States, the IAEA organized the first International Conference on Advances in Radiation Oncology (ICARO) to discuss and assess new advances in radiation oncology in the context of the physical and economic challenges facing all countries. The success of that conference led the IAEA to organize the second International Conference in Advances in Radiation Oncology (ICARO-2), held in Vienna from 20 to 23 June 2017, with the main goal of providing an overview of the issues facing radiation oncology today and examining the role of advanced technologies. The topics addressed included quality assurance, clinical practice, high precision radiotherapy techniques, stereotactic techniques, and the challenges and successes of implementing new radiotherapy technologies.

ICARO-2 drew some 400 participants from 95 Member States and 17 organizations. The conference comprised 69 sessions with 169 oral presentations, and included teaching lectures, e-contouring workshops and e-poster displays. This publication summarizes the topics addressed, the discussions, and the main conclusions and recommendations of the conference regarding the future of radiation treatment.

The IAEA officer responsible for this publication was E. Zubizarreta of the Division of Human Health.

CONTENTS

1. INTRODUCTION

1.1.BACKGROUND

As the longevity of populations increases continuously, cancer becomes a more prominent disease [1]. The increased incidence of cancer translates into an ever-increasing demand for health services. Health services associated with cancer require extensive equipment and personnel resources that can be challenging since Resources for both systemic and localized therapies require a significant investment and infrastructure.

Radiation therapy can be a cost-effective method of treating cancer if the appropriate diagnostic and therapeutic equipment are made available. Radiotherapy is often unavailable in many low-income (LI) countries throughout the world [2–3]. The International Atomic Energy Agency's (IAEA) Directory of Radiotherapy Centres (DIRAC) database reveals that in high-income (HI) countries, the ratio of treatment machines to population may be as high as six per million individuals, whereas in many low- middle-income-countries (LMI), the ratio is as low as one per 10–70 million individuals [4–5]. Many LI-countries often have only standard radiotherapy equipment and few qualified and trained staff. In addition, there are 36 Member States that have no radiotherapy services at all.

The IAEA organized the second International Conference on Advances in Radiation Oncology (ICARO-2) held in 2017, following the success of a similar conference held in 2009 [6]. The advances in radiotherapy technologies in the last few years have been striking, although numerous challenges are still to be faced, including achieving access to a high standard of cancer care in many countries. New radiotherapy techniques have been implemented over the past 8 years, such as advances in three-dimensional conformal therapy, stereotactic radiotherapy, intensity modulated radiation therapy (IMRT), image guided radiation therapy (IGRT), treatment planning, brachytherapy and unsealed-source techniques, proton and heavy-ion therapy, and quality assurance (QA) practices and standards. The increased use of complex techniques, coupled with the need to treat more patients in a shorter period, will continue to drive the reliance on technology, automation, and efficient QA verification of these clinical technologies that can impose a financial burden on health care programmes. Implementation of complex technologies in LMI-countries presents unique challenges beyond the financial burden, such as availability of adequately trained personnel, and appropriate infrastructure including for repair and maintenance of equipment.

1.2.OBJECTIVE

The aim of the conference was to discuss and define the current role and future potential of technological, medical physics and molecular/biological innovations for their incorporation into routine clinical practice in radiation oncology. It also provided a forum where advances in technology, best practices and quality assurance methodologies were disseminated and scientific knowledge exchanged. The objective of this publication is to present a summary of the topical sessions and to highlight the main conclusions and recommendations that were outcomes of the discussions at the conference

1.3.SCOPE

The scope of the conference was to provide clinicians, scientists and other professionals with an overview of technological achievements in the field of advanced radiotherapy techniques and of their potential future therapeutic benefits, as well as with a summary of progress made in the molecular/biological modification of tumour and normal tissue responses, and of advances in medical physics. The scope of this publication is to disseminate the impact of new technological and biological tools in current clinical practice and the possibility for future integration of the knowledge and tools in radiotherapy, preferably using clinical trials, as a suitable matrix for providing robust data for future clinical implementation.

1.4.STRUCTURE

This publication summarizes the topics addressed at the ICARO 2, it gives a review of the main topic areas discussed at the conference and highlights the main conclusion of each topic at the end of each section.

The structure of this publication, follows the structure of the conference, taking in to account the main topics discussed:

- Global Challenges and Resources in Cancer Treatment;
- Clinical Practice;
- Physics Practice and Quality Assurance;
- Implementation Challenges;
- Debate;
- Training and Educational Sessions;
- Poster Highlights;
- Conclusions.

2. CONFERENCE OBJECTIVES

The objective of the ICARO-2 meeting was to provide an overview of issues facing modern radiation oncology with an emphasis on advanced technologies and topics such as quality assurance (QA), clinical practice, high-precision radiotherapy techniques, stereotactic techniques and challenges/successes of implementing new radiation therapy technologies (Table 1). There were special sessions on new developments and trends, clinical applications of small field dosimetry, health care economics, automation in radiation therapy and paediatric radiation oncology. Workshops on e-contouring in treatment planning were organized. Parallel sessions for medical physics and clinical practice were given by international experts in the radiation therapy community and included side events to discuss very specific issues such as QA in clinical trials, comprehensive audits and collaboration with industry. There were also invited speakers who specifically addressed the challenges faced by LMI-countries in the implementation of new radiation therapy technologies. The conference had the following specific objectives:

— To review the current and future potential of technological, medical physics and molecular/biological innovations for clinical use in radiotherapy;

— To explore the applications of improved imaging tools in treatment planning;

— To review the current status of evidence-based recommendations for the treatment of common cancers;

— To review the latest developments in medical dosimetry and dose auditing procedures for new radiotherapy techniques;

— To review the current status of comprehensive audits in radiotherapy;

— To review resource sparing approaches in clinical radiotherapy practice;

— To exchange information on the current advances and implementation challenges in the field among leading experts;

— To define future challenges and directions in the clinical use of radiotherapy.

TABLE 1. OVERVIEW OF CONFERENCE CONTENT AND PROGRAMME TOPICS

Global Challenges and Resources in Cancer Treatment	• Global Challenge and the Role of Radiotherapy • IAEA Directory of Radiotherapy Centers (DIRAC) Database • Requirements for Safe and Effective Transition to New and Appropriate Radiotherapy Technology • Health Economics of Cancer • Education and Training • The Role of International Organizations and Professional Societies • Global Impact of Radiation in Oncology (GIRO)
Clinical Practice	• Breast, Cervix, Prostate, and Head & Neck Cancer • Personalized medicine • Towards a Radical Treatment of Oligometasteses • Combined Therapies including Immunotherapy • Brachytherapy
Physics Practice and Quality Assurance	• Quality in Radiotherapy: various dimensions • Imaging for Planning and Treatment delivery in EBRT • Quality Assurance (QA) from Simulation to Delivery • Quality and Safety • Small Field Dosimetry • Introduction to new ICRU report of 89 and 91
Implementation Challenges	• Access to High Quality Care: Challenges and Possible Solutions • Practical Implementation of New Technologies in LMI-countries • Future Trends in Radiotherapy
Debate	• Should IMRT be the Standard of Care?
Training and Educational Sessions	• e-Contouring – Lung, Breast, Head & Neck, GYN • Paediatric Radiotherapy • From GTV to PTV: Volume definition and Delineation • Radiotherapy Plan Competitive Initiative • Past, Present and Future of Brachytherapy • Quality Assurance (QA) for Modern Radiotherapy Techniques • Telemedicine • Translational radiation biology • How to evaluate a treatment plan • Automation in Radiotherapy
Poster Highlights	• Clinical poster highlights • Physics poster highlights • Radiobiology poster highlights

3. GLOBAL CHALLENGES AND RESOURCES IN CANCER TREATMENT

The conference was opened by Aldo Malavasi (Deputy Director General), Dazhu Yang (Deputy Director General) and May Abdel-Wahab (Director-NAHU) who addressed the 391 delegates from 95 different countries. The IAEA's role in the use of nuclear technology (cancer therapy, nuclear medicine and diagnostic radiology) in the support of human health has grown over the years [7] and has played a pivotal role in the treatment of cancer through four pathways:

— Addressing the need for quality assurance (QA) in diagnostic imaging, nuclear medicine and radiation therapy including audits at over 1000 radiotherapy centres;
— Training and education of radiotherapy professionals in LMI-countries;
— Making technical and educational resources freely available on the IAEA's websites; and
— Producing numerous guidance documents and educational publications worldwide [8].

Conferences such as ICARO-2 provide a venue for networking where healthcare professionals can come together to discuss and share knowledge. The Agency aimed to bring together experts from around the world as part of Coordinated Research Projects (CRPs) and the Technical Cooperation (TC) programme to assist LMI-communities in the diagnosis and treatment of cancer. Training of personnel through TC continues to be one of the IAEA's top priorities. Countries also have the opportunity to take advantage of many Agency resources such as the IAEA/World Health Organization (WHO) Secondary Standards Dosimetry Laboratory (SSDL) network, the IAEA/WHO dosimetry audit service and training materials (published and made available on the Human Health Campus website [9].

Since there is one goal to treat cancer even more effectively and safely across the world, there is a continuous need to 'bridge the gap' between need and implementation. Therefore, one of the key components of the ICARO-2 conference was to allow for an open interaction between healthcare personnel, industry and experts from all over the world to stimulate this process.

Two perspectives, those of a Radiation Oncologist and a Medical Physicist, were given regarding the changes that have occurred in the 8-year period since the first ICARO. Overall, at least fifty percent of cancer patients would benefit from radiation therapy. While radiation therapy is a fundamental and effective therapy for cancer patients, it is virtually absent from the global health discussion. Advances in radiation therapy have included, higher target conformity to further reduce normal tissue complications, and the use of (molecular) biology to enhance its therapeutic benefit. Other technological advancements include Image-guided radiotherapy (IGRT), MR-LINACS, Volumetric Arc Therapy (VMAT), proton therapy, molecular imaging, stereotactic techniques such as Stereotactic Body Radiotherapy (SBRT), hypo-fractionation, etc. Additional advances in radiobiology research, with the use of molecular targeted therapy, radio-genomics for personalized radiotherapy and immunotherapy which could be a paradigm shift for cancer care, have all been observed since the first ICARO conference. Even with all these rapid developments there is still a concern that many LMI-countries have little or very basic diagnostic and treatment facilities. Although palliative treatment is still common, there is an increasing number of curative patients. It is expected that the demand for radiotherapy services in LMI-countries will increase dramatically over the next 20 years.

Conclusion: The rapid development of radiation therapy in the past 8 years, increased awareness of its need and actions to address global disparities in access to radiation therapy services continue to be a priority. The IAEA-ICARO meetings represent a step in this direction.

3.1.GLOBAL CHALLENGES AND THE ROLE OF RADIOTHERAPY

In light of the global challenges and disparities in the availability of radiation therapy in LMI-counties, a panel of experts were convened to discuss the challenges in cancer care and the role that radiation therapy can play. The number of global cancer cases over the next 18 years is predicted to be higher in LMI-countries than in HI-countries [10]. There is an 'Equity Gap' in cancer care between LMI-countries and HI-countries in terms of availability of care, affordability and awareness (education, stigma). To address this gap, there is a need for more evidence based and technology driven innovation, political advocacy and a broader engagement of healthcare and cancer control organizations/programmes within each country. To accomplish these tasks, sustainability is required. A balance between essential needs, population growth and the limited resources (social organization and state of infrastructure) available within each country is needed to achieve sustainability. Key components to a sustainability framework include local environmental support, funding stability, partnerships, organizational capacity, program evaluation, program adaptation, communication and strategic planning. The need for implementing new radiation therapy programmes in LMI-countries is essential to address the projected growth in cancer incidence 20 years from now. Accessibility to radiotherapy technology will require innovation and forward thinking such as the ideas behind the suggestion of "BOXCare", where radiation therapy could be supplied at a scale needed and quickly [11]. However, any implementation of (new) radiation therapy technology, today and in the future, comes with a cost that requires appropriate funding models and support as well as the need to be able to deliver 'quality' treatments without making errors.

Conclusion: The need for a defined sustainability framework is essential in order to support the cancer healthcare needs in LMI-countries if the global cancer challenge is to be overcome.

3.2. IAEA DIRECTORY OF RADIOTHERAPY CENTRES (DIRAC)

An important resource for demonstrating the number of institutions with radiotherapy machines globally is the Agency's DIRAC database [5]. The DIRAC database has information from nearly 7000 radiation therapy centres across 139 countries. LMI-countries are shown to have only 10% of the teletherapy machines yet serve more than 50% of the global cancer population. There are 36 Member States that have no radiotherapy services at all.

Conclusion: The DIRAC database highlights disparities across geographical areas and economy levels and indicates the deficit in radiotherapy equipment needed for cancer treatment in LMI-countries. It is necessary to sustain the quality of the DIRAC database so that it can be used reliably for estimating radiotherapy resources.

3.3. REQUIREMENTS FOR SAFE AND EFFECTIVE TRANSITION TO NEW/APPROPRIATE RADIOTHERAPY TECHNOLOGY

As new radiation therapy technology and treatment innovations are introduced, the support from therapists, medical physicists, radiation oncologists and informatics staff are required. At the very beginning of the process, a response by administrators/decision makers, and professionals in leadership roles to appropriate questions is needed. Without the involvement of the appropriate people and answers to the relevant questions, the project is at a huge disadvantage Moreover, there are a number of proficiencies needed for the successful addition of new technologies such as image analysis, volume definitions, motion management, etc.

The therapists (RTTs) are key team members in any transition to new technology since they are the ones who are the final safety check prior to treatment. Their understanding of how the technology functions and its ultimate aim is essential, and thus education and training is essential and must be provided first. to the addition/introduction of Intensity Modulated Radiation Therapy (IMRT) is not ‘a simple process’.

Conclusion: Transitioning to new technology and treatment modalities requires input from decision makers and the radiation therapy team before final decisions are made. Before implementation, ROs, MPs and RTTs need to be educated and trained in the new technology.

3.4. HEALTH ECONOMICS OF CANCER

The expectation is, that with new technologies one can transform efficacy to efficiency to availability and finally to distribution of these technologies which ultimately results in positive outcomes. The challenge is to make treatments effective and affordable. Data from HI-countries show that as effectiveness increases, cost also increases. There is currently a scarcity of studies that analyze the real cost of treatments. Clinical trials have been assumed to be an ideal way to study cost, but because they are designed for a very specific population and not for the general population, they do not necessarily result in true indicators of average cost. An example of an “ideal costing” study was conducted in Belgium where SBRT was being delivered even though it was not being reimbursed. The study showed that SBRT was feasible and cost effective, and a reimbursement scheme was implemented [12].

Conclusion: None of the new technologies or treatment modalities can be implemented without additional financial support. To fully understand the cost vs. effectiveness, more validated evidence on both costs and outcome need to be collected. Utilize the potential of innovative reimbursement strategies for early adoption of innovative radiotherapy technologies to stimulate the generation of evidence. Healthcare policies should be designed to maximize the health of the country’s population with the means that are available.

3.5.EDUCATION AND TRAINING/ ROLE OF INTERNATIONAL AND PROFESSIONAL SOCIETIES

There are numerous scientific and professional organizations providing assistance in the development of education and training programmes. Presentations from 18 different groups in two sessions were presented to demonstrate the resources available, and the efforts that have been made to enhance the treatment of cancer patients with radiation therapy.

The IAEA has provided numerous publications that are readily available from their websites [8], e.g. a recent IAEA publication provides guidelines for implementing a new radiation therapy machine and includes check sheets of all the components that must be considered prior to purchase and implementation [13].

Numerous considerations are required to be understood such as what are the internal (infrastructure, IT support, financial and regulatory) versus the external (education, QA/safety culture and staffing levels) requirements and how they influence implementation. Without fully understanding all these requirements, there can be an increase in technology but not an increase in patient accessibility.

The European Society of Therapeutic Radiation Oncology (ESTRO) through their “Schools” has a long history of providing access to continuing education and personal/professional development. The International Centre for Theoretical Physics’ (ICTP) has introduced an advanced international postgraduate medical physics master’s program for students, mainly from LMI-countries. The International Organization for Medical Physics

(IOMP) has contributed to education and professional standards of medical physics such as defining what the requirements are to become a “qualified” medical physicist. The Latin American Association of Medical Physicists (ALFIM) described its efforts to implement Brazil’s national training program for MPs. Efforts to enhance national education programs in three different countries (Canada, Romania, Saudi Arabia and the USA) were presented. Canada has shifted to a competency-based model of curriculum development, Romania now employs a competency-based education system for RTTs, Saudi Arabia implemented an international radiation therapy plan competition and the USA described efforts to provide an online competency-based education and training program in radiation therapy.

Next to education and training also other activities were highlighted such as: exchanging knowledge, partnerships, fellowships, regional co-operation, preparation of guidelines etc. The representatives from JASTRO (Japanese Society of Therapeutic Radiation Oncology), FARO (Federation of Asian Organizations for Radiation Oncology), and SEAROG (South East Asia Radiation Oncology Group) presented their activities in Asia, while AFROG (African Radiation Oncology Group) and ALATRO (Ibero-Latin-American Society of Radiation Oncology) are active in Africa and Latin America respectively. ESTRO (European Society for Radiotherapy and Oncology), ASTRO (American Society for Radiation Oncology), UICC (Union for International Cancer Control) and ABS (American Brachytherapy Society) conduct many global activities.

Conclusions: Active support / support from international organizations and the IAEA regarding training of the entire radiotherapy team remains very important. Their efforts will undoubtedly lead to a better treatment of cancer patients.

3.6.GLOBAL IMPACT OF RADIATION IN ONCOLOGY

The topic of Global Challenges on implementing radiation therapy in LMI-countries was highlighted in one of the last sessions of the conference where the Global Impact of Radiation in Oncology (GIRO) was discussed [14]. GIRO uses an evidence-based approach to focus on radiation therapy access in a meaningful and affordable manner to generate practical applications/tools. This approach looks, at the same time, at both the specific details of the country as well as details of the disease to understand how to close the gap between access and need. A great deal of effort has focused on defining cost/benefit to treat the top ten cancers. For each country and each cancer type, the radiation therapy delivery model, current treatment capacity, how many fractions are needed versus what is available, the operation cost per fraction, and the investment required to generate a new fraction had to be analyzed to determine what was needed to meet the demand. The estimated cost of global expansion of radiotherapy to provide full access to treatment in 2035 is $184 billion. Even though the initial investment would be high, the long-term benefit to each country would also be high since more lives would be saved and that would translate into higher per capita productivity. Five calls for action came from these analyses [15]:

- Population based cancer control plans must be developed;
- Expand access to radiation therapy;
- Develop the human resources needed for radiation therapy;
- Obtain sustainable financing;
- Align radiation therapy access with local healthcare providers.

With these actions it is believed that the gap between need and accessibility can be closed in 2035. However, when examining the accessibility of radiation therapy across the 5 worldwide regions, it was observed that there is 204% capacity in North America compared to only 31% in Africa. Access to radiation therapy and sustainable expansion in Asia and Africa represent the biggest problem. The gap has grown over the past 10 years between HI-countries and LMI-countries. The care of cancer patients in these LMI-countries is not limited to just radiation therapy but also to the whole field of cancer care where the challenges include lack of screening programs, high patient load with high stage IV disease, lack of trained human resources, limited pathology, limited radiology capacity, limited stocks of chemotherapy, significant treatment delays, lack of communication between public and private hospitals, no follow-up for treated patients, lack of relevant treatment guidelines, and lack of government commitment. These challenges are found across all LMI-countries and in order to overcome them there must be a global investment to treat this disease and prolong the lives of many cancer patients.

Conclusions: LMI-countries need to prioritize resources in order to fight cancer more effectively. Global investment in RT can prolong life, improving the productivity and wellbeing of these nations.

4. CLINICAL PRACTICE

During ICARO-2 several sessions were dedicated to specific topics in clinical practice. In these sessions, experts presented topical overviews, followed by presentations of proffered papers from the participating Member States

4.1.BREAST CANCER

In radiotherapy for breast cancer, clinical target volumes for post-operative radiotherapy after breast conserving surgery are being established for: conserved breast, lymph node regions, and the tumour bed for boost. Hypo-fractionated regimens, which completes the whole treatment in approximately 3 weeks, with simple field in field forward planning Intensity Modulated Radiotherapy (IMRT) are becoming a standard for post-operative whole breast irradiation. Efforts such as “deep inspiration breath hold” [16] are being implemented worldwide to reduce the risk of late cardiac toxicities for these patients.

4.2.CERVICAL CANCER

In radiotherapy for cervical cancer, chemo-radiotherapy including brachytherapy, has been the standard of care for advanced disease. Recent developments in 3D image-guided brachytherapy, including the establishment of clinical target concept, prescription dose, and dose-volume constraints for organs-at-risk volumes (PRVs), has led to the improvement of clinical results [17]. Adoption of IMRT or IGRT in external beam radiotherapy is also being studied. More evidence in currently ongoing studies are expected to improve our understanding of dose-volume relationship of disease control and PRV toxicities. Selected papers on doses to involved lymph nodes in cervical cancer patients undergoing image-guided adaptive brachytherapy and multi-institutional clinical studies of chemo-radiotherapy for cervical cancer conducted in Asian countries, were presented.

4.3.PROSTATE CANCER

Radiotherapy, especially with the advancement of IMRT, is considered to be a major treatment modality for localized/locally advanced disease, and its combination with hormonal therapy (androgen suppression) has been investigated in many randomized trials to elucidate the optimal combination duration and strategy A study with a median follow up of 10 years where prostate-cancer–specific mortality was low, with no significant difference among treatments was presented. Surgery and radiotherapy were associated with lower incidences of disease progression and metastases than active monitoring [18]. The clinical results of Carbon-ion Radiotherapy (CIRT), advanced particle therapy technology showed better results than photons, particularly in high risk patients. Data presented were very promising; however, this technique is too expensive for many countries in the foreseeable future conventional approaches should continue being used.

4.4.HEAD & NECK CANCER

Head & Neck cancers are another disease group in which radiotherapy plays a major therapeutic role. The invited lecture on this subject presented the overview of presentations made in the American Society for Radiation Oncology Annual Meeting (ASTRO) in 2016. Current evidence from GORTEC 99-02 continues to support conventional once daily fractionation as the standard of care in chemo-radiotherapy for locally advanced Head & Neck cancer [19]. The authors also concluded that acceleration of RT does not compensate for radio-sensitization with chemotherapy. Data from an ongoing Phase II clinical trial on Attenuated

Chemo-radiotherapy for Human papillomavirus (HPV) positive locally advanced oropharyngeal cancer suggests that the radiation treatment regimen could be based on the response to chemotherapy. Multi-institutional analyses on IMRT- or Stereotactic body radiotherapy (SBRT) based re-irradiation for Head & Neck cancer have shown that "modern" re-irradiation techniques are associated with less severe complications and are better tolerated than conventional approaches to re-treatment. Selected papers on the experience of IMRT for Head & Neck cancer in India and the significance of Matrix metalloproteinases-1 (MMP-1) levels as a predictive marker for oral mucositis severity, were presented and discussed.

Conclusions: The awareness of late cardiac toxicities when using more advanced techniques in the RT of the left breast has led to concerns about reducing the dose and volume of the heart in the radiation field. In RT for cervical cancer, recent developments in 3D image-guided brachytherapy, including the establishment of the clinical target concept, prescription dose, and dose-volume constraints for PRVs, has led to the improvement of clinical results. The large number of trials on the treatment of localized prostate cancer clearly showed the importance of the different strategies and the role of RT in treating this disease. Current evidence from the GORTEC 99-02 continues to support conventional once daily fractionation as the standard of care in chemo-radiotherapy for locally advanced Head & Neck cancer [19].

4.5. PERSONALIZED MEDICINE

The concept of "Precision Medicine" or "Personalized Medicine" is emerging fast in the field of oncology. In this concept, biomarkers such as genetic markers are used in the prediction of clinical outcomes (predictive/prognostic markers) and selection of therapy (response markers) mainly chemotherapy. However, it is expected that personalized treatments will have implications for radiotherapy in the future [20]. The number of publications on "Biomarkers" and "Radiation Oncology" has increased from about 400 per year in the year 2000 up to about 1300 per year in the year 2015. The global molecular biomarkers market is estimated to reach USD 53.34 Billion by 2021 from USD 27.95 Billion in 2016. Current research on the genomic assays and their clinical impacts and complexities were presented and discussed. When a specific marker has been identified, it needs to be validated and at the end of the testing, the most important step, is to prove its clinical utility.

Conclusions: While the concept of personalized medicine has strong implications in the field of chemotherapy, its implication for radiotherapy may emerge in the future.

4.6.TOWARDS A RADICAL TREATMENT OF OLIGOMETASTASES

The concept of "oligometastases", which is the presence of a limited number of metastatic sites and lesions, was initially presented in 1995 [21] and is receiving more attention recently [22] Recent studies on patients with oligometastases treated with surgery or radiotherapy, especially Stereotactic Body Radiotherapy (SBRT) or Stereotactic Ablative Radiotherapy (SABR), are providing evidence that these patients may benefit from the addition of these local treatments not only by prolonging survival but by also achieving long-term survival [23–24]. The characteristics of these patients such as the type of primary disease, site of the metastatic lesions, and period of disease-free status, may be important in selecting patients who may benefit from the additional local therapy. Technical aspects of SBRT or SABR such as precise imaging, patient alignment, motion/deformation management, and interpretation of composite plans, need to be considered for effective implementation.

Conclusions: Oligometastases could represent a new indication for radiotherapy in the future.

4.7.COMBINED THERAPIES INCLUDING IMMUNOTHERAPY

Radiotherapy is often combined with systemic therapy such as chemotherapy in order to control cancer. In a "classical" sense, this has been due to the spatial consideration that radiotherapy is a local modality and adding systemic therapy, can improve the overall efficacy [25]. Current studies are showing that the effectiveness of the combination may also come from the biological effect of radiotherapy especially in its combination with immunotherapy. Many studies on the combination of check-point blockade immunotherapy and radiotherapy, often in a form of SBRT with high-dose hypo-fractionated regimens, are underway. Previous studies seem to indicate that the addition of immunotherapy may induce the abscopal effect (anti-cancer effect of radiotherapy outside the irradiated volume) [26].

Selected papers on chemo-radiotherapy for HIV (Human Immunodeficiency Virus) positive patients with Stage IIIB cervical cancer; the effect of skin reaction in the selection of patients with Head & Neck cancer that are treated with Cetuximab; and a combination therapy of endoscopic infusion of radio-sensitizer with chemo-radiotherapy for advanced rectal cancer, were presented and discussed.

Conclusions: More clinical trials using radiotherapy combined with systemic therapy, including immunotherapy need to be designed/conducted to investigate its efficacy and possible toxicity.

4.8.BRACHYTHERAPY

Brachytherapy continues to be a very valuable radiation technique in LMI-countries. In the session on brachytherapy, five presentations on different approaches to enhance brachytherapy treatment were given. These advances included image guidance, new catheter placement techniques, innovative training methods and development of dose to water standards for electronic brachytherapy. Image guidance for cervical cancer treatment with brachytherapy was shown to improve the placement of sources to achieve better target coverage. Other presentations focused on the safety and quality aspects of brachytherapy treatments. For example, one study investigated on whether one can simply interchange low dose-rate prostate brachytherapy sources from different seed manufacturers without compromising quality of such treatments? The authors concluded that one should not do this without performing appropriate clinical calibration and dosimetric evaluation. This example could provide guidance to centres in the LMI-countries who may not have the resources to perform such research work and yet may be tempted to simply interchange sources without knowing the consequences of such an action.

Conclusions: Advances in brachytherapy imaging, planning, and delivery require careful planning as they are implemented.

5. PHYSICS PRACTICE AND QUALITY ASSURANCE (QA)

During the ICARO-2 conference there were numerous sessions and discussions on Medical Physics practice and the need for the appropriate Quality Assurance (QA) to support accurate and safe radiation therapy delivery. A key presentation was given as a basis for understanding the need for "quality" radiation therapy. The goal within radiation therapy dose delivery is to deliver the prescribed doses within a ±5% window as described in the ICRU 24 report [27] and supported by clinical evidence. Examples were given showing different outcomes, poorer tumour control and greater normal tissue complications, when patients received doses outside of the 5% window. Analyses of many different clinical trials also have supported the strong need for accurate and quality radiation therapy.

5.1. QUALITY IN RADIOTHERAPY: VARIOUS DIMENSIONS

5.1.1. Quality Assurance Team for Radiation Oncology (QUATRO)

The IAEA has implemented numerous audits to assist radiation therapy centres in LMI-countries to review their radiation therapy practices, and to offer recommendations on how to improve. One of the most prominent IAEA audits is the Quality Assurance Team for Radiation Oncology (QUATRO) comprehensive audit which began 10 years ago. This audit program is most active in Europe, but centres elsewhere in the world have also requested and completed QUATRO audits [28]. A key component of the audit report is that it not only focuses on the weaknesses of each centre but also on their strengths [29]. One of the key findings were, shortages of staff and equipment in 50% of the audited centres. Specific examples of QUATRO audits were presented by Qatar and Serbia where both representatives agreed that the audit was very beneficial and that they considered it to be an essential quality improvement tool.

5.1.2. Reduction of Errors

Another mechanism for improving quality in radiation therapy is to reduce errors and treatment times, while improving cost and efficiency. The Institute for Safe Medical Practices (ISMP) [30] identified "automation" as a top-ranking quality management tool that can help reduce errors and thereby improving quality of care. Presentations were given showing that automated commissioning of treatment planning systems can reduce errors and time when compared to manual commissioning of Treatment Planning Systems (TPSs), thereby improving quality, cost and efficiency of the treatment process. Other presentations show that automation in the treatment planning process can select complex Volumetric modulated arc therapy (VMAT) radiosurgery plans that are comparable in plan quality to those generated by experienced planners. The auto planning is shown to save up to 3 hours per VMAT plan, a considerable saving in time and improvement of cost and efficiency.

5.1.3. Quality Assurance Programmes

The delivery of quality radiation therapy depends on many different factors ranging from having trained qualified personnel and appropriate functioning equipment, to good clinical practice and QA programs. There are many other factors as well. Several of these factors were highlighted in a series of presentations covering subjects about: information technology and data flow support in a radiotherapy department; this included looking at what is needed to move a large radiation therapy department from one location to another; considerations for purchasing radiation therapy equipment, and experiences with QUATRO. Critical elements for all these components included communication with all interested parties, development of quality management (QM) systems, and clarity in the responsibilities of each radiation therapy staff member.

5.1.4. Training

Despite the recognition that there is a need and high demand for Clinically Qualified Medical Physicists (CQMPs) around the globe, particularly in the LMI-countries, the infrastructure to train CQMPs is not well developed. IAEA has published documents describing resources and programmes that will be needed to develop such infrastructures [31]. There were presentations from the Federation of African Medical Physics Organizations (FAMPO) who assessed the suitability of radiotherapy centres to offer FAMPO accredited clinical training of medical physicists among 25 centres in 11 countries. Their study showed that FAMPO accredited medical physics clinical training programmes in Africa would improve the quality and the number of CQMPs who would readily be in position to practice competently and independently. This in turn would contribute to improved radiation treatment delivery leading to improvements in quality of care to cancer patients. It is agreed that there is a need to increase accredited medical physics clinical training programmes all over the world. The work by FAMPO [32] is a great step in that direction for the African countries.

Conclusions: Important mechanisms for improving quality in RT are: Regular audits (i.e. QUATRO), error reduction and reduction of treatment times by using automation; development of QA programmes, training and accreditation, and good communication between all personnel. Education and training programmes can be run successfully in resource-constrained environments.

5.2. IMAGING FOR PLANNING AND TREATMENT

As new radiation therapy technologies are implemented in LMI-countries there must be the recognition that with these “sophisticated” treatment modalities, the requirement for quality imaging is critical. Conforming the dose to the target while minimizing the dose to the normal tissues requires precise identification of each volume during the treatments. To achieve quality images, there are several desirable characteristics that should be considered such as soft tissue contrast, faster imaging protocols, affordability, lower radiation dose to the patient, etc. Imaging is not only used for identification of structures, but also accounting for motion, size changes, and relevant molecular extension of the disease. High quality images also allow for the precise calculation of the dose by the treatment planning systems (TPS). Image Guided Radiation Therapy (IGRT) provides a useful tool to better identify what to irradiate and what not to irradiate during a course of radiation therapy treatment.

IGRT requirements include a link to treatment planning with reference imaging and contours, integration into the treatment machine, appropriate contrast (MRI is the current ultimate contrast machine), fast to be commensurate with treatment times and organ changes and allowing for re-planning with complex IGRT. Moreover, images should be low dose and hence of low risk. Future challenges to incorporating imaging into radiation therapy will include deformable registration, critical structure identification and interpretation of biological imaging.

Additional presentations covering PET-CT for lung cancer, the role of the RTT in IGRT, image registration methodologies, prompt gamma imaging for proton therapy and digital portal imaging for ^{60}Co radiation therapy were given. The use of PET-CT for lung tumours has the benefit of reducing the irradiated volume but difficulties with image quality for target delineation need to be resolved. A key component to any IGRT process includes education of the RTTs. They should be trained in all the various imaging modalities that could be used during radiation therapy.

Since ^{60}Co units are still widely used in LMI-countries, the idea of obtaining ^{60}Co portal images was presented along with the challenges of low contrast. Different techniques were used to improve contrast but not to the same level as kV images.

Conclusions: Advances in imaging technologies will lead to improved treatment delivery (better definition where the tumour is) and the development of new techniques in radiation oncology.

5.3. QUALITY ASSURANCE FROM SIMULATION TO DELIVERY

Each radiation therapy treatment consists of a chain of processes that must all be accomplished correctly for the final delivery of the radiation dose to be effective. This chain of processes generally includes the initial simulation, treatment planning, patient set-up, and dose delivery. This radiation therapy chain actually may be comprised of 100s of small details that contribute to an accurate delivery of the therapeutic dose.

The IAEA, as part of its Coordinated Research Projects (CRPs), has developed and provides various audits to LMI-countries to verify specific components of the chain. One such audit is a postal audit of the reference beam output in 132 different countries [5]. Current results show that >95% of the beams audited fall within the 5% criterion. Beyond the reference output audit, the Agency has developed several other audits that span from relative dosimetry to complex dosimetry to end-to-end quality assurance audits for IMRT. Another example of an IAEA initiated quality assurance (QA) audit is a coordinated research project (CRP) for IMRT that focuses on “Development of quality audits for advanced technology radiotherapy dose delivery”. The purpose of this CRP was to verify transfer of an IMRT treatment field to the treatment unit, delivery of the treatment field, and the agreement between the relative dose distribution delivered and calculated by the treatment planning system.

The Imaging and Radiation Oncology Core (IROC) Houston Quality Assurance (QA) Centre is another centre that provides numerous quality audits. As complex and new technology is implemented in radiation therapy centres, it is difficult to fully understand and verify all of their components. Therefore, end-to-end QA audits are performed using anthropomorphic phantoms. Several systematic errors have been detected and corrected using these end-to-end QA audits such as errors in lung dose calculations, inappropriate modelling of Multi Leaf Collimator (LC) leaf ends and proton dose calculation errors. Other QA centres such as the Radiotherapy Trials Quality Assurance (RTTQA) Centre also provides audits for both simple and complex radiation therapy delivery. All QA centres develop their QA audits to be effective and efficient yet yield accurate and precise results. Information was presented on new virtual audit techniques using methods in which centres provide digital data back to the QA centre for analysis instead of using postal and on-site audit methods. Quality indicators are used to assess and verify that the correct treatment is delivered. These indicators should include treatment plan quality (dose objectives, DVH [dose-volume-histogram] analysis), dose delivery, and treatment plan robustness. It is important to verify the entire process and not just one component.

Conclusions: Introduction of new technologies present challenges that need to be verified prior to treating patients. In this context it is very important to conduct audits to detect discrepancies. The use of End-to-end QA phantoms will help detecting errors, to improve dose delivery accuracy and will provide confidence.

5.4.QUALITY AND SAFETY

Development of an overall quality management (QM) programme is a requirement for implementing any new radiation therapy technology or treatment modality. Traditionally, QM programmes are prescriptive in nature, but currently there is a movement to a Failure Modes and Effects Analysis (FMEA) process. The American Association of Physicists in medicine (AAPM) has adopted this FMEA process and describes it in their TG-100 report [33]. TG-100 takes a proactive approach to quality management by defining QA as radiation therapy procedures are implemented. This approach requires the staff, as a team, to map the process, perform a failure mode and effects analysis, followed by a fault tree analysis, and then develop a QM programme based on risk (the product of severity, lack of detectability, and probability of occurrence scores) of each failure mode.

An FMEA describes what might happen, whereas an incident learning system (ILS) describes what happened. With an ILS the processes can be re-designed to avoid any risks without implementing new Quality Control (QC) procedures. More reporting in an ILS leads to safer treatments since they stimulate discussion and actions that are specific to that particular centre. There are several incident learning systems available to the radiation therapy community such as the AAPM's safety profile assessment survey, ASTRO's RO-ILS or the IAEA's SAFRON. Learning from our mistakes not only improves the accuracy of radiation therapy delivery but also improves patient safety as described by the Bonn Call-for- Action.

Conclusions: Using Failure Modes and Effects Analysis (FMEA) in combination with incident learning (IL) will provide an improved overview of risks within the different aspects of the treatment of patients with radiotherapy.

5.5. SMALL FIELD DOSIMETRY

Several of the new radiation therapy treatment modalities, stereotactic, radiosurgery (SRS) and Intensity-modulated radiotherapy (IMRT), all include the use of small radiation fields. The measurement and calculation of radiation doses for these small fields is a "very difficult" process. In the clinic, the question always arises what kind of detector should be used to measure both reference dose, field output factors and relative dose distributions, both for commissioning new equipment as well as for performing patient-specific measurements, such as SRS and Stereotactic Body radiotherapy (SBRT) Quality Assurance (QA). Results of studies presented at the meeting provided guidance to the medical physics community on the commercially available detectors and phantoms that are suitable for performing patient specific SBRT-QA.

The IAEA and the American Association of Physicist in Medicine (AAPM) recognized the difficulties associated with small field dosimetry and developed a Small Field Dosimetry Code of Practice (CoP) as TRS-483 [34] An entire educational session was devoted to specific details of this CoP. The CoP addresses reference and relative small field dosimetry for photon beams up to 10 MV. The conditions and definitions for small field dosimetry determination were presented and examples of how to choose the correct detector were presented. For relative small field dosimetry, there is no ideal chamber, but there are suitable detectors. The user must also consider volume averaging and perturbation corrections for accurate measurements. As the field sizes decrease, the correction factors can be quite large (6-7%). It was shown that it is critical that the ion-chamber/detector must be setup in the water tank so that it is aligned to the centre of the field where maximum signal is achieved. A general description of the formulism, dose measurements, and calculation options was given.

Implementation and further development of the Small Field Dosimetry CoP required effort to determine appropriate chamber correction factors as well as testing of the CoP in the clinical setting. Several presentations were given describing the generation of correction factors for various detectors on various treatment machines. Data were presented for 14 different detectors on three different machine types. All of the studies were in agreement and showed that application of the CoP brought all of the results much closer resulting in better output factors. Further testing of the variability in the results when a single correction factor was used for 10 detectors of the same make and model, was conducted. These data indicated that there could be variations in the correction factors of ±1.5%. Verification of the CoP for various machines for both reference and non-reference conditions using various different detectors at up to 13 different radiation therapy centres was performed to test the CoP. Measured output factors differed somewhat for field sizes of $\leq 1 \times 1 cm^2$ due to not following the CoP strictly and not using the "recommended" detector.

Conclusions: A known dosimetry issue has been addressed with the new CoP that will improve the accuracy in the dosimetry of radiation therapy for small fields. The recommendations from this study were that more than one detector should be used for these small field measurements and that the CoP should be followed explicitly. It was also shown that detector selection is of crucial importance.

5.6. INTRODUCTION TO NEW ICRU REPORT OF 89 AND 91

5.6.1. ICRU Report 89

The International Commission on Radiation Units & Measurements (ICRU) has released a report on: Prescribing, Recording, and Reporting Brachytherapy for Cancer of the Cervix [35]. This report starts with the essential background, including a clinical introduction, historical and current techniques (e.g., volumetric imaging for cervical cancer). An important element is the introduction of the 4D-adaptive target concept at specific times for treatment based on clinical examination and imaging. For the organs at risk (OARs) next to the target, the report emphasizes the presence of different morbidity endpoints and related substructures in the organ. The radiobiology chapter explains the limitations of the linear quadratic (LQ) model but encourages the use of the EQD2 concept as the current best option for treatment planning and overall dose reporting. A detailed concept is recommended to report dose and volume parameters related to contours and reference points. The report contains detailed chapters on treatment planning, particularly for the three-dimensional volumetric approach, but also the underlying concepts of dosimetry that remain essential for volumetric and radiography-based planning.

5.6.2. ICRU Report 91

This report is prescribing, recording, and reporting of Stereotactic treatments with small photon beams [36]. Rapid developments in imaging and radiation-delivery technology have stimulated the use of small photon beams in stereotactic radiation therapy (SRT). Historically, stereotaxy refers to the use of a three-dimensional coordinate system to localize intracranial targets and has recently been extensively developed in extracranial clinical situations. SRT includes stereotactic localization techniques combined with the delivery of multiple small photon fields in a few high-dose fractions. In SRT, the therapeutic ratio is optimized through delivery of highly conformal absorbed dose distributions with a steep dose fall-off achieving an optimal absorbed dose in the target volume in combination with minimal normal-tissue irradiation. Consistent with earlier ICRU Reports this report recommends a strict definition of target volumes (GTV, CTV) by reviewing imaging modalities used in clinical practice. This report deals with the basic principles of small-field dosimetry, algorithms for treatment-planning, commissioning, and quality assurance (QA) for the existing delivery systems, as well as the role of image guidance during delivery. Finally, it recommends a framework for prescribing, recording, and reporting stereotactic radiotherapy, and deals with most of the pathologies eligible for stereotactic delivery (malignant and non-malignant).

Conclusions: Both ICRU reports provide important guidelines for further improvement of the treatment of cervical cancer with brachytherapy, and the use of SRT in the treatment of brain tumours.

6. IMPLEMENTATION CHALLENGES

Several presentations were dedicated to “Access to High Quality Care”, “Practical Implications of New Technologies” and “Future Trends in Radiotherapy”.

6.1. ACCESS TO HIGH QUALITY CARE: CHALLENGES AND POSSIBLE SOLUTIONS

6.1.1. Survey

To gain some general knowledge as to what the radiation therapy needs are within LMI-countries, the IAEA conducted a survey that was sent to 78 radiotherapy centres all over the world. There were 27 responses primarily (81%) from MI-countries. The findings indicate that MI-counties are not interested in “low-level technologies”. These countries want the same technology as what is currently used in HI-countries such as IMRT, IGRT, and VMAT. Understanding this desire and the future trends in radiation therapy technology is a real challenge for the IAEA and International Health organisations regarding what techniques to implement, over the next decade. However, the top barriers for implementation of these advanced techniques are lack of professional staff, lack of training, and lack of funding. The key steps to overcoming the barriers are: to engage and educate the appropriate decision makers (hospital administration and/or government officials), and to partner with industry and professional/scientific organizations to provide training and financial support.

Conclusions: Implementation of new technologies or techniques in LMI-countries will be a challenge for the next decade.

6.2. PRACTICAL IMPLEMENTATION OF NEW TECHNOLOGIES IN LMI-COUNTRIES

Several sessions were devoted to the challenges for implementing new radiation therapy technology or modalities. Presentations on the practical implementation and access to new technology in LMI-countries, with personal experiences from several different countries, were given. Experiences with implementation and accessibility within Ghana, Turkey, Canada, India, Zambia and Asia were discussed. Accessibility to radiation therapy technology varied strongly between the LMI-countries.

A good example of developing high quality care in a LMI-country is India. I.e. within this country, Stereotactic Radiation Surgery (SRS) is being implemented in several institutes and “end-to-end” QA phantoms to verify radiation dose delivery are being developed. Other important developments are access to maintenance/spare parts and appropriately trained staff. On the other hand, within Ghana, there are only three radiation therapy centres to handle 30,000 patients. Recently they introduced 3D conformal radiotherapy (CRT). Although the transition was successful different barriers have to be solved in the future including lack of access to CT imaging, lack of government commitment, limited treatment planning system workstations and a serious backlog of patients. In Zambia, only one radiation therapy centre is active and a couple of satellite facilities are being planned. A key component to gaining accessibility to radiation therapy has been the engagement with the government to provide funding and resources. A key limitation throughout all of Africa is the lack of trained staff. It is one of the Agency’s priorities to assist in providing training opportunities to radiation therapy professionals in African countries. Within Asia the IAEA is running a programme on the implementation of Image guided HDR (high-dose-rate) brachytherapy in 15 countries. A total of 121 radiation oncologists and medical physicists were trained in this new technique. However, several countries faced difficulties in the implementation of this technique due to limited access to imaging devices, lack of treatment planning systems, lack of trained staff, lack of funding and heavy workload. Turkey has a long history of providing "good quality" radiation therapy services, yet their primary limitation is not funding or commitment of the government but a shortage of RTTs and medical physicists. Even in Canada, a HI- country, issues regarding accessibility to radiation therapy are evident because of the geographic location (long distances) of services versus populations in need. Inequitable access to RT, despite adequate resources and universal health insurance is a challenge for the Canadian Radiotherapy community to be resolved.

Conclusions: There are many common factors that contribute to accessibility barriers such as: lack of personnel/facilities, lack of training/education, lack of government commitment and lack of funding.

6.3.FUTURE TRENDS IN RADIOTHERAPY

A series of four lectures discussed future trends in RT. The first presentation highlighted technological opportunities. For example, MRI-guided adaptive radiotherapy offers potential benefits that are tailored to the personalization of the treatment (simulation, planning, delivery, patient extraction and tumour function). This technique is feasible in daily practice, but further research and validation to define the potential is necessary. The second presentation specifically focused on challenges for LMI-countries. Such as re-defining "old" radiation techniques, reduction of "human errors" (will automation be helpful?), introduction of hybrid professions (imaging/oncology/tech), and finally, concentrate manpower on high risk modalities, and use a standardized approach wherever possible.

In several HI-countries there is an increase in number of centres offering particle therapy. As long as the number of centres is still limited: the issue is not whether particle therapy is superior, but which indications and subgroups of patients will benefit most, given that for the foreseeable future particle therapy will remain a scarce treatment modality. Designing and building smaller facilities could reduce treatment costs and possibly lead to a stable reimbursement system and established and accepted indications for treatment. The last presentation focused on the Japanese experience with Carbon-ion (C-ion) RT. In the last 2 decades, more than 24,000 cases were treated with C-ion RT at 10 carbon ion facility all over the world. It was found that C-ion RT led to better local control and survival in many radio-resistant advanced tumours.

Conclusions: Sparing normal tissues and reducing side effects, without compromising the effectiveness of the treatment remains an important task for the radiotherapy community. Personalized treatment, use of MRI-guided RT as well Particle therapy are candidates for the future to reach this goal.

7. DEBATE: SHOULD IMRT BE THE STANDARD OF CARE?

One of the highlights of the ICARO-2 conference was a debate on ***"Should IMRT be the standard of care?".*** This debate included two prominent radiation oncologists and two prominent medical physicists. The clinician arguments supporting the statement, described the benefits of normal tissue sparing, target conformity, and achieving higher tumour doses with less toxicity. The clinician arguments against the statement, focused on the difficulty in implementing Intensity-modulated radiotherapy (IMRT) as evidenced by audits and clinical trials showing equal survival outcomes between IMRT and 3D conformal radiotherapy, and uncertainties in contouring thereby negating the gains achieved in conformity to the target. The physicist in support of the proposal argued that, dose conformity is a key element in delivering better radiation therapy with IMRT but admitted that training and expertise were needed to implement IMRT accurately. The physicist opposing the proposal described the possible errors that could happen if IMRT was not implemented correctly pointing to errors in small field dosimetry and the catastrophic nature of incidents in highly complicated treatments.

After additional discussion by the panelists and audience it was decided that every step of implementing IMRT has to be looked at very carefully. To deliver the highest quality IMRT, accurate structure contouring is required. Any transition to a new treatment delivery modality such as IMRT requires a learning curve by the staff that should emphasize the need for attention to every detail. Indications should be developed and followed, appropriate training provided, published guidelines for commissioning followed, a QA programme that allows independent audits developed and resources for preventive maintenance ensured. The creation of clinical protocols identifying the appropriate disease sites to be treated with IMRT and monitoring the outcomes of the treatment should be a priority prior to implementation.

Conclusion: At the end of the debate it was agreed that Intensity-modulated radiotherapy (IMRT), if approached cautiously, could be the standard of care for appropriate cases as long as adequate resources, support and funding are available.

8. TRAINING AND EDUCATION

The training and educational session consisted of teaching lectures, lunchtime workshops, demonstrations and symposia. The lecture on the Past, Present and Future of brachytherapy gave a nice overview of the progress of this technique over the years. Other lectures were on Quality Assurance (QA) for Modern Radiotherapy Techniques; From GTV to PTV: Volume definition and Delineation; How to evaluate a treatment plan; and Translational radiation biology. During this session (1) Mechanisms of "deterministic" radiation effects was presented; (2) Preclinical research into basic mechanisms of Radiation Related Heart Disease; and (3) The current status (power and weaknesses) of Radiogenomics was discussed. During the symposia on pediatric radiotherapy and telemedicine, the latest technology applied in pediatric radiotherapy was presented, and the feasibility of telemedicine in the field of radiotherapy in LMI-countries was discussed, respectively. A Demo session was organized on the subject of Radiotherapy Plan Competition Initiative and Automation in Radiotherapy.

Inconsistencies in contouring target and critical structures can seriously undermine the precision of (conformal) radiation therapy planning and are generally considered to be the biggest and most unpredictable source of errors in radiation oncology. Four workshops on e-Contouring were given including: Lung tumours, Head & Neck cancer, Breast cancer, and Gynaecological tumours. The objectives were: to learn how to contour the Gross tumour volume (GTV) and Clinical tumour volume (CTV), and Organ-at-risk (OAR) in these tumours.

Conclusions: Sessions on Training and Education are very important in order to improve the knowledge and skills of the attendees.

9. POSTERS

Electronic-Posters (e-Posters) were on display throughout the conference. e-Poster presentations were held during the coffee breaks. 5 screens (5 posters per screen) were available, 4 sessions in the mornings and 3 in the afternoons were assigned to poster presentations. A total of 175 posters were presented.

9.1.CLINICAL POSTER HIGHLIGHTS

Six clinical posters were selected to be highlighted during the meeting. One of those six was selected as the best poster for an award. Six selected clinical posters are described below:

(1) The first poster from Malta presented an “Audit of patient waiting time” in order to target the causes of radiation treatment start delays. They found that the process of contouring and planning was the primary causes of long waiting times. As future steps, the study team will focus on identifying and implementing potential solutions.

(2) The second study from Romania reported on “The risk of 2^{nd} primaries in cancer survivors”. They found that one out of 10 cancer patients suffered a 2^{nd} primary. Hence, appropriate follow-up and counselling regarding cancer risk factors is critical for survivorship planning and follow-up care.

(3) The third study from Tunisia evaluated “Survival and prognostic factors in non-metastatic breast cancers”. This was a retrospective study of 474 patients diagnosed between 1994-2004. Stage II was the most common stage at presentation, and the majority of patients had axillary lymph nodes involved. The median follow-up was 93 months, and the overall survival (OS) at 5 years was 74%. Factors associated with OS were hormonal status and extra-capsular extension. Interestingly, between 1994 and 2004, OS improved by 20% and was likely due to increased efforts to improve early diagnosis!

(4) The fourth abstract was from IAEA and presented outcomes of an “IAEA expert panel on relevance and implications of competency-based radiation oncology education in LMI-countries”.

(5) The fifth poster from Iraq presented a study evaluating the “Feasibility of hypo-fractionated adjuvant radiation for breast cancer (27 Gy in 5 daily fractions)” in the context of war and limited resources leading to long waiting times (8 months on average.) 30 patients were treated on this protocol to breast or chest wall, +/- regional lymph nodes. According to the authors this regimen was feasible.

(6) The sixth and final poster was the award-winning poster. This was a randomized study from Egypt studying “The effect of hypofractionated radiation in paediatric patients with diffuse intrinsic pontine glioma (DIPG)”. Paediatric patients were randomized to 54Gy/30 fractions vs. 39Gy/13 fractions vs. 45Gy/15 fractions. There was no difference in overall survival (OS) or progression-free survival (PFS) at 18 months. The authors concluded that given that there is no difference in outcome, patients should be treated with hypofractionated regimen.

9.2.PHYSICS POSTER HIGHLIGHTS

Five posters were selected and highlighted on different subjects:

(1) The first presentation was from FAMPO/IAEA on: "Africa Accreditation of Medical Physics Clinical Training Program in Africa: Survey of FAMPO and IAEA". There is a need to increase accredited MP clinical training programmes all over the world. This African initiative is a great step in that direction and will lead to improvement in the quality and quantity of trained personnel (CQMPs) who would readily be in position to practice competently and independently and contribute to improved radiation oncology treatment delivery.

(2) The second presentation was from Brazil on: "Low dose-rate prostate brachytherapy: do different seeds manufacturers matter?" Their goal was to investigate whether a simple interchangeability of sources from different manufacturers is feasible without the appropriate clinical calibration and dosimetric evaluation. The authors concluded that a simple interchange ability of sources from different manufacturers is not recommended without the appropriate clinical calibration and dosimetric evaluation

(3) The third presentation was from the USA on: "Automated treatment planning system commissioning: Error reduction and improved efficiency" The aim was to investigate whether a FMEA technique of an automated commissioning test suite will improve the quality of commissioning when compared to a manual commissioning process. The authors found that results of FMEA for the automated commissioning suite show reduced risk for failure modes and a reduced number of failure modes over the current TPS commissioning guidelines. Use of an automated commissioning process will improve quality by reducing errors and time, while improving cost and efficiency. Comment from the reviewer: There has been much discussion at the conference on the discussion of FMEA technique for various processes. A nice work that shows how FMEA tools can lead to efficiency and cost savings while at the same time improve quality.

(4) The fourth presentation was from Cuba on: "Quality audit of IMRT treatment planning using EBT3 film and RPL Glass dosimetry system". The main results of INOR's participation in the IAEA CRP project E2.40.18 on "Development of Quality Audits for Advanced Technology I Radiotherapy Dose Delivery" were presented in this work. The purpose of the CRP was to verify transfer of an IMRT treatment field to the treatment unit, delivery of the treatment field, and the agreement between the relative dose distribution delivered and that calculated by the treatment planning system. The combination of RPL-GD/EBT3 seems to be an adequate alternative for performing the recommendations of the CRP. The results showed a 3% and 2% difference between the calculated dose and measured dose in the PTVs, on the Elekta Synergy and Precise accelerator respectively. There has been much discussion at the conference on the discussion of FMEA technique for various processes. A nice work that shows how FMEA tools can lead to efficiency and cost savings while at the same time improve quality.

(5) The award-winning poster was from Thailand on: "Patient-specific quality assurance evaluation for stereotactic volumetric modulated arc delivery using 6FFF beams" In the clinic the question always arises what kind of detector one should use to measure dose distribution for patient-specific QA for SBRT treatments. The purpose of their

study was to compare the dosimetric evaluation of lung SBRT plans in patient-specific QA using various detector types. The authors concluded that use of the ArcCHECK is possible for dose verification in SBRT case with high accuracy if the planning target volume (PTV) is not too small. This work will give confidence to the users that one can use ArcCHECK for dose verification for SBRT cases with high accuracy if the PTV is not too small.

9.3.RADIOBIOLOGY POSTER HIGHLIGHTS

When compared to Clinical and Physics poster sessions, the number of radiobiology posters was limited. Radiobiology posters concerned two "*in vitro*" studies, one "*in vivo*" animal study, and a total of nine translational radiobiology/clinical studies. These studies included five posters on modelling/treatment plans/calculation tools, two posters on the use of biomarkers in the treatment of cancer, and two on the use of novel treatment modalities and design of new trials.

The award-winning poster was from Cuba on the use of "Biomarker Predictors of Radiotherapy Response in Head and Neck Tumour". The main goal of their study was to recognize the relation between tumour response and expression of these biomarkers. In this study a set of biomarkers (EGFR, Ki67, Bcl2 and P16) were evaluated in 50 patients that received radiotherapy for Head & Neck cancer. The authors reported that a positive EGFR, Ki67 and Bcl2 was associated with tumour progression, poor survival and a more aggressive behaviour of the tumour. However, it is too early to use these markers in a predictive setting.

10. CONCLUSIONS

Rapid developments in radiation therapy over the past 8 years have highlighted the necessity to address global disparities in access to radiation therapy services. The IAEA-ICARO conferences represent a step towards decreasing this gap and supporting global efforts by providing collective recommendations on some of the most important needs when addressing these global disparities. The following are the conclusions of the ICARO-2 conference:

- The need for defined sustainability frameworks is essential in order to support the cancer healthcare needs in LMI-countries if the global cancer challenge is to be overcome;
- The DIRAC database highlights disparities across geographical regions and economic levels, indicating deficit of radiotherapy equipment needed for cancer treatment in LMI-countries. It is necessary to keep the DIRAC database updated and at a high level of quality to ensure it can be used for various radiotherapy data analyses;
- Transitioning to new technologies and treatment modalities requires input from decision makers and the radiation therapy team before final decisions are made. Before implementation, ROs, MPs and RTTs need to be educated and trained in the new technology;
- New technologies or treatment modalities can only be implemented with financial support. To fully understand the cost vs. effectiveness, more validated evidence on both costs and outcome need to be collected. It is important to utilize the potential of innovative reimbursement strategies for the early adoption of innovative radiotherapy and to stimulate evidence generation;
- Active support / support from international organizations and the IAEA for the training of the entire radiotherapy team remains very important. These efforts will undoubtedly lead to the improved treatment of cancer patients with radiation therapy.in LMI countries;
- LMI countries need more financial support in order to fight cancer more effectively. Global investment in RT can prolong life, as well as improve the productivity and wellbeing of these nations;
- Deliver the highest quality and value of care to cancer patients with the available resources is mandatory regardless of the equipment available or technique implemented.
- The awareness of late cardiac toxicities in the RT of breast cancer has led to many techniques reducing the dose and volume of the heart in the radiation field. In RT for cervical cancer, recent developments in 3D image-guided brachytherapy, including the establishment of clinical target concept, prescription dose, and dose-volume constraints for organs-at-risk (OARs), has led to the improvement of clinical results. The large number of trials on the treatment of localized prostate cancer clearly showed the importance of the different strategies and the role of RT in treating this disease. Current evidence from the GORTEC 99-02 continues to support conventional *once daily* fractionation as the standard of care in chemo-radiotherapy for locally advanced Head & Neck cancer;
- Clinical trials remain the gold standard to show changes in outcomes using these new technologies and techniques, although they are slow to change practice;
- While the concept of personalized medicine is a strong implication in the field of chemotherapy, its implication for radiotherapy may emerge in the future;
- Patients with oligometastases may present a new group of patients who will be indicated for radiotherapy in the future;

- More clinical trials using radiotherapy combined with systemic therapy, including immunotherapy need to be designed/conducted in order to investigate its efficacy and possible toxicity;
- Advances in brachytherapy delivery, while not as fast as for external beam radiation therapy, continue and it will require careful planning as they are implemented in LMI countries;
- Important mechanisms for improving quality in RT are: Regular audits (i.e. QUATRO), error reduction and reduction of treatment times by using automation; development of QA programmes, training and accreditation, and good communication between all personnel;
- Advances in imaging technologies will lead to improved treatment delivery (better definition of the location of the tumour) and the development of new techniques in radiation oncology;
- Introduction of new technologies present challenges that need to be verified prior to treating patients. In this context it is very important to conduct audits to detect discrepancies. The use of end-to-end QA phantoms will help detect errors, improve dose delivery accuracy and will provide confidence;
- Using Failure Modes and Effects Analysis (FMEA) in combination with incident learning (IL) will provide an improved overview of risks within the different aspects of the treatment of patients with radiotherapy;
- A known dosimetry issue has been addressed with the new CoP that will improve the accuracy in the delivery of radiation therapy for small fields. The recommendations from this study were that more than one detector should be used for these small field measurements and that the CoP should be followed explicitly. It was also shown that detector selection is crucial;
- Both ICRU reports provide important guidelines for further improvement of the treatment of cervical cancer with brachytherapy, and the use of SRT in the treatment of brain tumours;
- There are many common factors that contribute to accessibility barriers such as: lack of personnel/facilities, lack of training/education, lack of government commitment and lack of funding;
- Sparing normal tissues and reducing side effects, without compromising the effectiveness of the treatment remains an important task for the radiotherapy community. Personalized treatment, use of MRI-guided RT as well as particle therapy are candidates for the future to reach this goal;
- At the end of the debate it was agreed that intensity-modulated radiotherapy (IMRT), if approached cautiously, could be the standard of care if the right resources and funding are available;
- Sessions on Training & Education are very important to improve the knowledge and skills of the attendees.

APPENDIX. I. ICARO-2 STATISTICAL REPORT

Organizer:	IAEA
Co-operating organizations:	▪ European Society for Therapeutic Radiology and Oncology (ESTRO) ▪ International Cancer Expert Corps (ICEC) ▪ American Association of Physicists in Medicine (AAPM) ▪ International Organization for Medical Physics (IOMP) ▪ Japanese Society for Radiation Oncology (JASTRO) ▪ American Brachytherapy Society (ABS) ▪ Federation of Asian Organizations for Radiation Oncology (FARO) ▪ International Agency for Research on Cancer (IARC) ▪ International Society of Radiographers and Radiological Technologists (ISRRT) ▪ Medical Physicists without borders (MPWB) ▪ South East Asian Radiation Oncology Group (SEAROG) ▪ International Union Against Cancer (UICC) ▪ International Commission on Radiation Units and Measurements (ICRU) ▪ African Radiation Oncology Group (AFROG) ▪ American Society for Therapeutic Radiology and Oncology (ASTRO) ▪ Asociación Latinoamericana de Terapia Radiante Oncológica (ALATRO) ▪ Asociación Latinoamericana de Física Médica (ALFIM) ▪ European Federation of Organisations for Medical Physics (EFOMP) ▪ Federation of African Medical Physics Organisations (FAMPO)
Location:	Vienna International Centre M-Building (BR-B/M1, M2, M3)
Date:	20-23 June 2017
Total No. of participants & observers:	445 (out of 540 pre-registered)
No. of participants:	391
No. of participants from Member States	308
No. of participants from organizations	83
No. of Member States	95
No. of organizations	17

No. of observers/exhibitors:	54
No. of Sessions:	49
No. of oral presentations:	169 (3 opening statements, 163 oral presentations, 3 closing statements)
No. of teaching lectures	6
No. of demo sessions	2
No. of e-contouring workshops	4
No. of lunchtime symposia	8
No. of e-posters	181
Scientific Secretaries:	E. Zubizarreta, A. Meghzifene/H. Delis (NAHU)
Scientific Support:	A. Polo, G. Loreti (NAHU)
Admin. Support:	R. Gomez Zaragoza (NAHU)
Conference Coordinator:	M. Khaelss (MTCD)
Exhibition Coordinator:	V. Jordanovska (MTCD)
E-Poster Coordinator:	O. Belyakov (NAHU)
TC Coordinator:	S. Walleczek (TCPC)
Proceedings:	Summary report to be published on Human Health Campus web site

Participants: 391
From Member States: 308

Albania	1	Malaysia	1
Algeria	3	Malta	2
Argentina	1	Mexico	6
Australia	8	Morocco	1
Austria	16	Myanmar	1
Azerbaijan	1	Nepal	1
Bahamas	1	Netherlands	1
Bangladesh	2	New Zealand	1
Belarus	1	Nigeria	3
Belgium	4	Pakistan	1
Brazil	9	Panama	1
Bulgaria	2	Peru	6
Canada	12	Philippines	15
Chile	5	Poland	2
China	2	Portugal	1
Costa Rica	1	Qatar	1
Croatia	1	Romania	6
Cuba	4	Russian Federation	8
Cyprus	1	San Marino	1
Czech Republic	7	Saudi Arabia	4
Denmark	2	Serbia	2
Egypt	5	Slovakia	2
Estonia	1	Slovenia	6
France	1	South Africa	8
Georgia	1	Spain	2
Germany	11	Sri Lanka	1
Ghana	3	Sudan	2
Greece	1	Sweden	3
Hungary	5	Switzerland	2
India	11	Thailand	5
Indonesia	6	TFYR Macedonia	3
Iran, Islamic Republic of	6	Tunisia	6
Iraq	3	Turkey	4
Ireland	2	Uganda	3
Israel	1	Ukraine	5
Italy	8	United Kingdom	6
Japan	10	United Republic of Tanzania	1
Jordan	1	United States of America	12
Kazakhstan	1	Uruguay	1
Korea, Republic of	2	Viet Nam	1
Kuwait	1	Zambia	1
Latvia	3	Zimbabwe	1
Lebanon	1		

From Organizations: 83

AAPM (American Association of Physicists in Medicine)	5
ABS (American Brachytherapy Society)	1
AFROG (African Radiation Oncology Group)	1
ALFIM (Asociación Latinoamericana de Física Médica)	4
ASTRO (American Society for Therapeutic Radiology and Oncology)	2
EFOMP (European Federation of Organisations for Medical Physics)	3
ESTRO (European Society for Therapeutic Radiology and Oncology)	14
FARO (Federation of Asian Organizations for Radiation Oncology)	1
IAEA (International Atomic Energy Agency)	18
IARC (International Agency for Research on Cancer)	1
ICEC (International Cancer Expert Corps)	5
ICRU (International Commission on Radiation Units and Measurements)	2
ICTP (The Abdus Salam International Centre for Theoretical Physics)	16
IOMP (International Organization for Medical Physics)	5
MPWB (Medical Physics for World Benefit)	1
SEAROG (South East Asian Radiation Oncology Group)	1
UICC (International Union Against Cancer)	1

REFERENCES

[1] THUN, M.J., DELANCEY, J.O., CENTER, M.M., JEMAL, A., WARD, E.M., The global burden of cancer: Priorities for prevention, Carcinogenesis **31** 1 (2010).

[2] YAP, M.L., ZUBIZARRETA, E., BRAY, F., FERLAY, J., BARTON, M., Global access to radiotherapy services: Have we made progress during the past decade? J. Glob. Oncol. **2** 4 (2016) 207-215.

[3] BARTON, M.B., ZUBIZARRETA, E.H., POLO RUBIO, J.A., Radiotherapy in small countries, Cancer Epidemiol. **50** (2017) 257–259.

[4] ROSENBLATT, E., et al., Radiotherapy capacity in European countries: An analysis of the Directory of Radiotherapy Centres (DIRAC) database, Lancet Oncol. **14** 2 (2013) e79–e86.

[5] INTERNATIONAL ATOMIC ENERGY AGENCY, DIRAC, Directory of Radiotherapy Centres, https://humanhealth.iaea.org/HHW/DBStatistics/DIRAC/

[6] SALMINEN, E.K., et al., A., International Conference on Advances in Radiation Oncology (ICARO): Outcomes of an IAEA meeting, Radiat. Oncol. **6** 11 (2011).

[7] ABDEL-WAHAB, M., ET AL., Assessment of cancer control capacity and readiness: The role of the International Atomic Energy Agency, Lancet Oncol. **18** 10 (2017) e587–e594.

[8] INTERNATIONAL ATOMIC ENERGY AGENCY, Educational Publications IAEA, https://www-pub.iaea.org

[9] INTERNATIONAL ATOMIC ENERGY AGENCY, Human Health Campus, https://humanhealth.iaea.org

[10] TORRE, L., et al., A., Global cancer statistics, 2012, CA Cancer J. Clin. (2015) **65** 87–108.

[11] JAFFRAY, D.A., et al., Global task force on radiotherapy for cancer control, Lancet Oncol. **16** 10 (2015) 1144–1146.

[12] LIEVENS, Y., OBYN, C., MERTENS, A.S., VAN HALEWYCK, D., HULSTAERT, F., Stereotactic body radiotherapy for lung cancer: How much does it really cost? J Thorac. Oncol. **10** 3 (2015) 454–461.

[13] INTERNATIONAL ATOMIC ENERGY AGENCY, Setting Up a Radiotherapy Programme: Clinical, Medical Physics, Radiation Protection and Safety Aspects, IAEA, Vienna (2008).

[14] LIEVENS, Y., et al., Global impact of radiotherapy in oncology: Saving one million lives by 2035, Radiother. Oncol. **125** 2 (2017) 175–177.

[15] ATUN, R., et.al, Expanding global access to radiotherapy, Lancet Oncol. **16** 10 (2015) 1153–1186.

[16] MORAN, J.M., et al., Accelerated partial breast irradiation: What is dosimetric effect of advanced technology approaches? Int. J. Radiat. Oncol. Biol. Phys. **75** 1 (2009) 294–301.

[17] TANDERUP, K., et al., Advancements in brachytherapy, Adv. Drug Deliv. Rev. **109** (2017) 15–25.

[18] HAMDY, F.C., 10-year outcomes after monitoring, surgery, or radiotherapy for localized prostate cancer, N. Engl. J. Med. **375** 15 (2016).

[19] BOURHIS, J., et al., Concomitant chemoradiotherapy versus acceleration of radiotherapy with or without concomitant chemotherapy in locally advanced head and neck carcinoma (GORTEC 99-02): An open-label phase 3 randomised trial, Lancet Oncol. **13** 2 (2012) 145–153.

[20] BENTZEN, S.M., et al., Biomarkers and surrogate endpoints for normal-tissue effects of radiation therapy: The importance of dose-volume effects, Int. J. Radiat. Oncol. Biol. Phys. **76** Suppl. 3 (2010) S145–S150.
[21] HELLMAN, S., WEICHSELBAUM, R.R., Oligometastases, J. Clin. Oncol. **13** 1 (1995) 8–10.
[22] WEICHSELBAUM, R.R., HELLMAN, S., Oligometastases revisited, Nat. Rev. Clin. Oncol. **8** 6 (2011) 378–382.
[23] MILANO, M.T., KATZ, A.W., ZHANG, H., OKUNIEFF, P., Oligometastases treated with stereotactic body radiotherapy: Long-term follow-up of prospective study, Int. J. Radiat. Oncol. Biol. Phys. **83** 3 (2012) 878–886.
[24] TIMMERMAN, R.D., HERMAN, J., CHO, L.C., Emergence of stereotactic body radiation therapy and its impact on current and future clinical practice, J. Clin. Oncol. **32** 26 (2014) 2847–2854.
[25] STEEL, G.G., PECKHAM, M.J., Exploitable mechanisms in combined radiotherapy-chemotherapy: The concept of additivity, Int. J. Radiat. Oncol. Biol. Phys. **5** 1 (1979) 85–91.
[26] GRIMALDI, A.M., et al., Abscopal effects of radiotherapy on advanced melanoma patients who progressed after ipilimumab immunotherapy, Oncoimmunology, **3** (2014) e28780.
[27] INTERNATIONAL COMMISSION ON RADIATION UNITS AND MEASUREMENTS, Determination of Absorbed Dose in a Patient Irradiated by Beams of X or Gamma Rays in Radiotherapy, ICRU Report 24
[28] IZEWSKA, J., et al., Improving the quality of radiation oncology: 10 years' experience of QUATRO audits in the IAEA Europe Region, Radiother. Oncol. **126** 2 (2018) 183–190.
[29] INTERNATIONAL ATOMIC ENERGY AGENCY, Comprehensive Audits of Radiotherapy Practices: A Tool for Quality Improvement; Quality Assurance Team for Radiation Oncology (QUATRO), IAEA, Vienna (2007).
[30] Institute for Safe Medical Practices (ISMP): http://www.ismp.org
[31] IAEA training programmes: https://www.pub.iaea.org/MTCD/Publications/PDF/Pub1610_web.pdf
[32] FAMPO: https://fampo-africa.org
[33] HUQ, M.S., et al., The report of Task Group 100 of the AAPM: Application of risk analysis methods to radiation therapy quality management, Med. Phys. **43** 7 (2016) 4209.
[34] INTERNATIONAL ATOMIC ENERGY AGENCY, Dosimetry of Small Static Fields used in External Beam Radiotherapy: An International Code of Practice for Reference and Relative Dose Determination, Technical Reports Series No. 483, IAEA, Vienna (2017).
[35] INTERNATIONAL COMMISSION ON RADIATION UNITS AND MEASUREMENTS, Prescribing, Recording, and Reporting Brachytherapy for Cancer of the Cervix, ICRU Report 89 https://icru.org/content/reports/prescribing-recording-and-reporting-brachytherapy-for-cancer-of-the-cervix-report-no-89
[36] INTERNATIONAL COMMISSION ON RADIATION UNITS AND MEASUREMENTS, Prescribing, Recording, and Reporting of Stereotactic Treatments with Small Photon Beams, ICRU Report 91 https://icru.org/content/reports/icru-report-91-prescribing-recording-and-reporting-of-stereotactic-treatments-with-small-photon-beams

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