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Value-based radiotherapy: A new chapter of the ESTRO-HERO project.

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Key words

value-based, radiotherapy, innovation, outcomes, evidence

Abstract

Radiotherapy interventions are rapidly evolving and improving, holding promise for better patient outcomes, yet at the possible detriment of higher societal costs. The ESTRO-HERO value-based radiotherapy project aims to develop a framework defining and assessing the

value of radiotherapy innovations, to support clinical implementation and equitable access, within a sustainable healthcare system.

Radiotherapy is one of the cornerstones of multidisciplinary cancer care, required by at least one out of two cancer patients, and improving local control, survival and quality-of-life [1-3]. Due to the increasing cancer incidence, the numbers of patients that will need radiotherapy are expected to further rise dramatically in the years to come [1,4]. Unfortunately, radiotherapy access remains far from optimal, especially in low-and middle-income countries, mainly due to the lack in human and capital resources [1,5]. Disturbingly, underutilisation also occurs in many high-income countries, in spite of better resource availability. In Europe, for instance, at least a quarter of the cancer patients who should receive radiotherapy, do not [3].

Over the past decades, radiotherapy has been evolving, innovating and improving at a rapid pace, holding promise for better patient outcomes [6]. This evolution however harbours the risk of a growing divide between the swift uptake of new radiotherapy interventions, even without strong evidence in some cases, and a remaining underutilisation of radiotherapy, negatively impacting the outcome of cancer patients. While imposing a choice between implementing innovation and providing optimal access is not at stake, it is mandatory to find common ground on how to define the real value of radiotherapy innovations, in order not to waste limited budget, and resources, further hampering access and the sustainability of health system financing.

Radiotherapy innovation

Innovative radiotherapy results from the evolution in radiation technology, but also from the integration of advanced imaging before and during radiotherapy, and the availability of high-performing computer systems [6]. This has led to the development of a broad range of new techniques, intensity-modulated (IMRT), stereotactic body (SBRT) and adaptive (ART) radiotherapy to name but a few. The increased potential of novel technologies and techniques to target the tumor, while limiting the dose – and toxicity – to the surrounding organs, has further paved the way to the adoption of new irradiation schedules (such as hypofractionation – fewer but higher doses per treatment) and new indications (e.g. oligometastatic disease, combinations with new systemic agents) [7-10].

Some innovations represent major changes with the potential to impact outcome in a stepwise fashion, think of new dose fractionation schedules, new radiotherapy-drug combinations or technologies with distinct biological, physical or imaging properties such as particle therapy or MR-guided radiotherapy. As in other aspects of cancer, innovation may however not be seen as a major breakthrough at onset, yet present itself as a series of smaller, incremental, changes of which the real impact gradually becomes evident over time [11,12]. Examples of the latter could be new immobilisation devices or computer planning algorithms.

Radiotherapy is unique in that the translation of innovation into improvements in outcomes – especially decreased toxicity and the consequential impact on quality-of-life – may only become apparent months to years after therapy. In addition, new radiotherapy techniques and technologies often require specific training, leading to learning curves, with outcomes dependent on operator-skill, the experience of the multidisciplinary team, and embedded

quality assurance processes [11]. Both factors translate into a time-dependency of radiotherapy innovations, where formal evidence of improved outcome may take long to mature.

How to support radiotherapy innovation

Innovation is taking place in all aspects of cancer care – often with shortening life cycles – which, along with the increasing incidence and burden of cancer, has resulted in an unprecedented growth of cancer care expenditure over the past decades [13,14]. In view of the need for financial sustainability, healthcare systems should focus on the introduction of those new cancer care interventions that are high-quality, efficient and equitable, by using dedicated health technology assessment (HTA), reimbursement and policy decisions [12,15]. Moreover, acknowledging that innovations should make a meaningful difference to patients, greater involvement of patients and caregivers in defining and assessing their value is needed. [12].

Alas, a strong HTA approach for innovation with medical devices, consistent with the one used for new (cancer) drugs, has yet to be developed, accepted and implemented in Europe [11,16]. This is not trivial. Innovative radiotherapy technologies and techniques may come at a cost, due to higher initial investments and the additional time and resources required to enable their safe and high-quality implementation and utilization [17]. In contrast, innovation in the preparation (e.g. through increasingly automated planning) and the delivery of radiotherapy may in turn facilitate optimized workflows, increase productivity and reduced treatment duration (such as through hypofractionation), which may counteract increasing costs.

The radiotherapy reimbursement systems in place to date do not sufficiently recognize the dynamic evolution of radiotherapy practice [18]. One illustrative example is that the majority of national reimbursement systems still support a fraction-based model, which is detrimental to the uptake of evidence-based hypofractionated radiotherapy schedules. Ideally, evidence on clinical benefit and cost-effectiveness, in addition to data on safety, of any new radiotherapy intervention should be rewarded by reimbursement that promotes its adoption in clinical practice. Data can be derived from prospective clinical trials, but due to the specificities of radiotherapy and the broad range in treatment indications being addressed, a blended approach to evidence generation, including real-world data should be considered [15,16,19].

While there is a tendency to propagate innovations on the pure belief that new is better, even if evidence remains limited and uncertain, the radiotherapy community – along with all relevant stakeholders including patients – should take up its responsibility and not accept a substandard evidence-base and small benefits of new radiotherapy interventions at whatever cost. In contrast, a strong healthcare system should embrace the delivery of innovative technologies, techniques and treatments that provide real value to the patients, at fair prices [15].

Value-based healthcare, a radiotherapy perspective

According to Porter, value-based healthcare (VBHC) is defined as the health outcomes (that matter most to patients) achieved per dollar spent over the total cycle of care [20]. Taking this notion of VBHC forward, value scales have been developed to appraise both the strength of clinical evidence and the expected added benefit for the patient of a particular intervention, whereas traditional cost-effectiveness or cost-utility tools tend to focus on whether an intervention meets a pre-defined threshold for cost per outcome [21]

With respect to value, changes in both outcomes and costs will enhance value. A pragmatic example to understand this is hypofractionation, a proven treatment approach in specific breast or prostate cancer indications [7,8,22]. Reducing the number of radiotherapy fractions, but achieving the same health outcomes across the life cycle, would be a high value intervention given the reduction in resource costs of treatment delivery and in treatment burden with potential quicker return to previous activities. Furthermore, some hypofractionated treatments may result in reduced toxicities, which over the cancer care cycle is likely to decrease healthcare and societal costs by lower need for interventions to manage these complications, or to enable individuals to partake in work and day to day activities [23,24].

As higher costs do not guarantee improved outcomes [25], initiatives have sought to define high and low value cancer care. These include prioritisation exercises by multi-stakeholder groups defining low-value or unsafe care practices in particular country or continent contexts, such as the Choosing Wisely campaigns [26-28], or the development of value appraisal tools for new interventions. With respect to the latter, the ESMO Magnitude of Clinical Benefit Scale, the ASCO Value Framework and the NCCN Blocks are the dominant scales that have been used when considering the value of oncology interventions, specifically drug treatments [29-31]. These value frameworks use a pre-defined rigorous approach to appraising evidence and aim to provide transparency for various stakeholders around the perceived benefits and required standards of new therapies. Importantly, they provide benchmarks for the level of evidence and magnitude of benefit to be considered for reimbursement, which should ultimately ensure evidence on new interventions is generated keeping the relevant outcomes in mind.

Some caveats to the use of these tools have however been raised: not all drugs appraised to be high-value also deliver the expected benefit in practice [32,33], nor do these frameworks grasp all intricacies that come along with surgical or radiation oncology [11]. In the latter, for instance, there are a broader range of outcomes to consider over and above overall survival or quality-of-life. These may include local control and organ preservation, but also functional aspects such as improvement in swallow function or conservation of speech for those with mouth cancers, or time to return to work. The appropriateness of these endpoints may vary significantly depending on the type of innovation and its intent.

Porter proposed to group outcomes into three tiers [20]. Following the same concept, clinical outcomes, specifically pertaining to the context of radiation therapy, have been suggested [34].

Tier 1 considers the health status achieved following treatment, incorporating both survival and the degree of health recovery, which for radiotherapy may include local control and functional outcome. Tier 2 focuses on the process of recovery, the time required to achieve remission or return to normal activities, and the burden of treatment on the individual with respect to acute toxicities and frequency or length of treatment. Tier 3 considers the sustainability of health or long-term consequences of care, including recurrences, sustained functional outcomes, long-term toxicities, complications and quality-of-life.

Ultimately, studies on new cancer interventions, be it drugs or loco-regional treatments, should not only consider the relevant outcomes depending on the type of intervention and the magnitude or degree of benefit [35], but should also use the right trial design to generate the evidence to support the given treatment modality, technology or technique. Indeed, innovations that can potentially improve outcomes in a stepwise fashion are likely to necessitate more robust prospective or randomised evaluation because of the effect on long-term survival, toxicity and quality-of-life; whereas this may not hold for innovations which represent incremental improvements and seek to improve efficiency, safety and usability. Evidence generation may therefore span from randomised controlled trials over pragmatic study concepts to real-world data collection, e.g. in a context of coverage with evidence development programs [12,15,36,37]. Whereas real-world data undoubtedly have an increasing role to play, particularly with respect to understanding long-term patient outcomes, adverse events and costs of care, their interpretation is very broad and not all of homogenous quality, hence guidance on what constitutes high-quality observational data is needed [38,39].

Finally, two other aspects are important to consider in VBHC, not in the least in the context of loco-regional cancer treatments such as radiotherapy. One is the notion of operator skills or provider quality, which may not only impact outcome, but also the resources required to deliver treatment. For that reason, one should incorporate aspects of health service delivery, such as resource use and related costs, into the evidence development process from the outset [11]. The costing part of the value equation has been largely neglected by the available oncology value tools and has been subject to limited evaluation to date. Yet it is extremely important in the field of radiation oncology where many studies have a non-inferiority design with interventions designed to achieve more efficient and cost-effective practices of care, without necessarily quantifying this or specifying the degree of effect sought.

ESTRO-HERO value-based healthcare project

Under the auspices of the Health Economics in Radiation Oncology programme of the European Society for Radiotherapy and Oncology (ESTRO-HERO) [40], a new project is launched aiming to develop a robust framework for the appraisal of radiation oncology innovations. As described, there are several conceptual challenges to achieving this goal [11,34]. Three key areas that need exploration and consensus building will be addressed as part of a multidisciplinary programme in order to ensure a framework that is evidence-informed, robust and able to handle the significant heterogeneity that exists within radiation oncology (figure 1).

1. *To define and categorise the spectrum of innovations in radiation oncology:*

This work-package will provide a method for classifying radiotherapy interventions. It will first categorise them broadly into technologies, techniques and treatments, before considering whether they represent stepwise or incremental innovations. This classification is crucial given the vast heterogeneity and volume of radiotherapy innovations that presently exists;

2. *To define the outcomes supporting the implementation of radiotherapy innovations:*

This work-package will focus on generic and tumourtype-agnostic outcomes relevant for radiotherapy. Clinical as well as patient-centred outcomes, along with economic outcomes – including operational and quality aspects – will be considered [41,42]. Whilst the HERO-VBHC project will not seek to develop or define new (sets of) outcome measures for specific tumour types, it will define which outcomes should be prioritised for new radiotherapy interventions, and categorise the diverse outcomes into tiers [11,34]. The evolving concepts of curative versus palliative treatment intent will also be considered to aid the categorisation;

3. *To define what magnitude of benefit and level of evidence is needed to support the clinical implementation of a particular radiotherapy intervention:*

This work-package will link the previous two by addressing the major conceptual challenge of combining the minimum benefit required and the minimum level of evidence needed to support the implementation of a particular radiotherapy intervention. The benefit will be determined by considering clinical, patient-centred and economic outcomes and the magnitude of benefit in each domain. In addition, for each intervention type the acceptable level of evidence will be defined and weighted according to the strength of the evidence.

Integrating all above aspects will allow to build a value-based framework for appraising radiotherapy innovations.

It is obvious that developing a value-based framework for radiation oncology, core in ESTRO's vision, will necessitate collaboration of all involved in the radiotherapy care pathway including radiation oncologists, physicists, and radiation therapists [43]. It is obvious that the input of patients will be invaluable in the definition and categorisation of the relevant outcomes and the minimal benefit that is deemed worthwhile [41,42]. Similarly, the expertise of epidemiologists, health economists and biostatisticians will be needed to define the required levels of evidence and for building the final value-based framework. While the ESTRO is committed to support and drive this initiative, endorsement from the multidisciplinary oncology community at large, and from a broad range of stakeholders involved in the treatment of cancer patients with radiotherapy, will be sought to help develop this project.

In conclusion, in an era of enhanced scrutiny on how to introduce innovative healthcare interventions into daily practice and to define their value, the radiation oncology community, supported by a broad group of stakeholders in the field of multidisciplinary oncology, will launch a project to define a VBHC framework considering the specificities of radiation oncology in terms of types of interventions and treatment intent, outcomes generated and evidence required. The HERO-VBHC project aims to develop such a framework in keeping the already existing tools and acknowledging the expertise that has been developed in this field.

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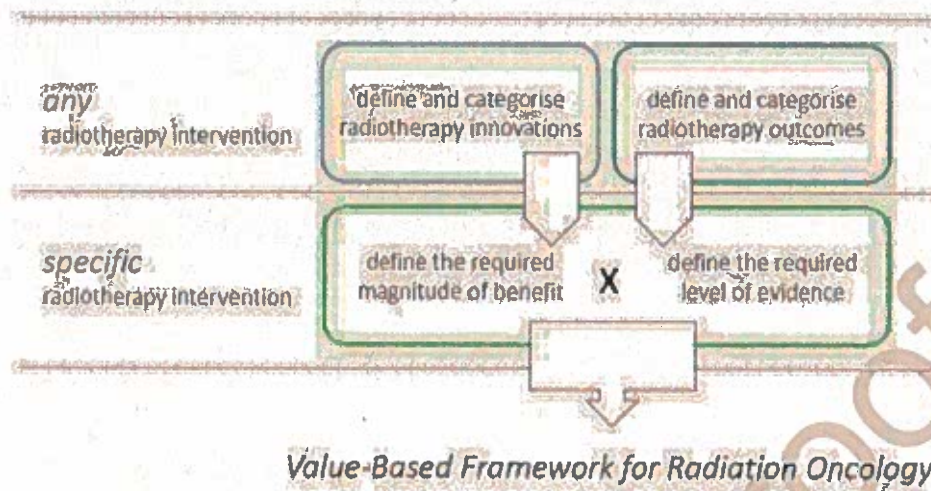
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Figure 1. ESTRO-HERO value-based healthcare project



Highlights

- Radiotherapy innovation consists of a broad spectrum of technologies, techniques and treatment approaches, that can represent stepwise or incremental changes
- Healthcare systems should support radiotherapy innovations that provide real value to the patients, at fair prices
- The appropriate evidence should be generated considering each type of innovation
- Current value appraisal tools for oncology do not sufficiently address outcomes relevant to support radiotherapy implementation
- The HERO-VBHC project aims to develop a value framework accounting for radiotherapy-specific aspects in terms of intervention type and intent, outcomes and required evidence

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