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Editorial

The role of ESTRO guidelines in achieving consistency and quality in clinical radiation oncology practice

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The aim of *Radiotherapy & Oncology* is to publish original research and topics of interest for radiation oncology. This includes publishing guidelines and recommendations from the European SocieTy for Radiation Oncology (ESTRO) groups focusing on e.g., target volume definitions, radiotherapy planning techniques and quality assurance, as well as on educational aspects including core curricula for the different professional groups forming our discipline. Since 2012 many of the clinical and technical guidelines have been under the auspices of the Advisory Committee for Radiation Oncology Practice (ACROP), now called the ESTRO Guidelines Committee (EGC). A search on Web of Science Nov 2nd, 2022, using search words "Radiotherapy and Oncology", "guideline or recommendation" and "ESTRO" revealed 259 manuscripts, and 59 of these were original guidelines. In total, these 59 ESTRO guidelines published during 1996–2022 had on average 118 citations each (Fig. 1). The top scoring guidelines are from the GEC ESTRO group [1,2] with > 1000 citations. Twenty guidelines have > 100 citations [1–20]. Thirty of the 100 most downloaded papers during 2021 from all papers ever published in *Radiotherapy & Oncology* were guidelines, and 18 of these were ESTRO guidelines (personal communication, the Elsevier office). The top-10 list of downloads identifies 7 as guidelines and 3 of them from ESTRO [4,21–26]. In addition, there are a number of ESTRO guidelines published in our sister journals and other journals. A basic principle of guideline development within ESTRO has been that wherever possible they should be evidence-based providing an authoritative view on each subject. Perusing the references cited at the end of recent guidelines reveals a substantial contribution from original articles published in *Radiotherapy & Oncology*. In some instances, and particularly when addressing radiotherapy technique, there may be no high-level evidence, and consensus guidelines are developed. ESTRO has a strong focus on developing, publishing, reading and evaluating guidelines for radiotherapy, and through the process which has evolved within ACROP, including a rigorous process of external peer review, the guidelines are a scientifically sound basis for the benefit of all patients. Importantly, it has been demonstrated that strict adherence to guidelines translates into better prognosis for patients [27,28]. Acknowledging the importance of guidelines, the ESTRO multidisciplinary teaching courses give a strong focus on our guidelines, which are discussed in detail and demonstrated in practical use [29–31]. Overall, ESTRO and the community can be proud of this work as we strive to do better for our patients, translating to better cancer outcome and less late morbidities. *Radiotherapy and Oncology* values guidelines and is proud that many of them have been published in our journal. We also offer co-publishing of guidelines and archiving important guidelines otherwise not publicly available as supplementary materials to original publications.

However, is it sufficient to simply produce ESTRO guidelines and to hope, or even state, that they are being used? The first guidelines from the GEC-ESTRO group were validated and reported upon recently in the EMBRACE-I cohort study, where investigators reported results using the guidelines for target volume definition,

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but the dose levels and number of fractions were per institutional guidelines [32]. Several studies on radiation associated late morbidities have been reported from the EMBRACE-1 study [e.g., 33–37], and this has translated into the interventional EMBRACE-II prospective study, where the ESTRO guidelines now must be followed [38]. These impressive studies deserve acknowledgement for ensuring a unified approach to target volume contouring and reporting. However, this did not necessarily imply a unified treatment or proof of better outcome. It is therefore not sufficient to use ESTRO guidelines and recommendations on target definition and planning; it is pivotal that they are validated, with initiation of further clinical trials.

When the ESTRO consensus for target volume determination in early breast cancer was published in 2015, the phase III randomised trials DBCG Skagen trial 1 (NCT02384733) and HYPOG-01 (NCT03127995) were initiated to test the use of moderately hypofractionated loco-regional radiotherapy in high-risk breast cancer [4]. Both trials specified that the target volume definition should be per ESTRO guideline, and both tumour outcome and late effects will be reported accordingly. Most ESTRO guidelines are unfortunately not defined as a prerequisite in prospective trials, and most patients (more than 95 %, https://hints.cancer.gov/docs/Briefs/HINTS_Brief_48.pdf) are not included in prospective trials [39], in part due to not meeting eligibility criteria [40]. However, phase IV studies may contribute valuable information with a high degree of detail and it is also possible to collect the full exposure data (CT-, structure-, dose- and plan-DICOM files) from large numbers of patients for analysis.

Alongside the ESTRO guidelines, *Radiotherapy & Oncology* regularly publishes papers from trial groups on quality assurance with over 1000 manuscripts in the past 10 years including those from EORTC, RTOG, SIOP and GHG. We have therefore a rich source of detailed radiotherapy data on which to base our practice. Validation of such data derives from the trial results and in evidence–based practice application of trial data to accomplish reproduction of the radiotherapy techniques used. These experiences have also highlighted the need for rigorous peer review and structure definition to minimize variation between clinicians in volume definition and several have highlighted educational approaches to optimize reproducibility.

Accurate, consistent and high-quality planning and delivery of dose with rigorous dose reporting is hugely important for the understanding of biology. Differences in a late effect may be misinterpreted as being due to a more or less sensitive patient, whereas it may actually be due to a different given dose. Moreover, valuable phenomena observed in preclinical studies potentially allowing treatment optimisation, such as shifting of ED50 with inhomogeneous dose, interactions between organs, regional differences, hypersensitive areas in tissues and low dose hypersensitivity [41] will never be verified in clinical studies and large data sets without a high level of quality assurance and correct dose and dose localization reporting.

In recent years, an increasing number of studies have used artificial intelligence to contribute to the development of personalized radiotherapy, e.g., based on genomics, radiomics, dosiomics and clinical parameters [42–44]. While several guidelines on the execution and reporting of such studies exist, e.g. [45–48], general methodological issues often remain, for example due to limited feature reproducibility and robustness, non-standardized feature pre-processing and under-reported model development, missing external, multicentre, and prospective validation, limited risk-assessment of the obtained predictions or limited clinical interpretability and accessibility for patients and clinicians. *Radiotherapy and Oncology* offers the possibility to publish guidelines related to specific problems of data analysis in the format of Data Sciences Briefs, for example the topic of model validation [49] and competing-risk analysis [50].

Besides encouraging their use, it is also important to monitor compliance with published guidelines, and capture potential variations in implementation: for example, institutions could claim to be using ESTRO contouring guidelines but actually implement them differently and – intentionally or not - introduce modifications and hence disparities in practice. Therefore, workshops are necessary to teach and reinforce the proper interpretation of con-

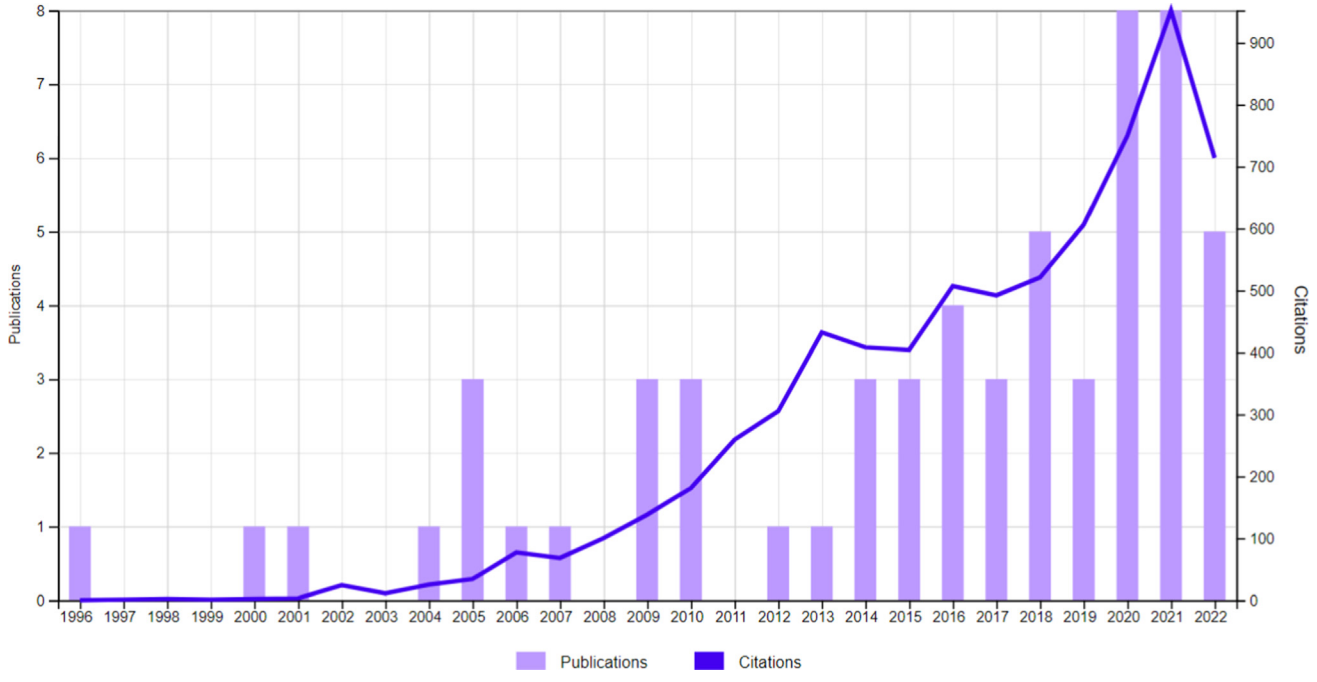

Fig. 1. Web of Science, Nov 2nd, 2022, using search words "Radiotherapy and Oncology", and "guideline or recommendation" and "ESTRO". In total 259 hits, and 59 of these were original guidelines or recommendations. Here is listed number of publications per year of publication and total number of citations.

touring guidelines [51,52]. Furthermore, it has been suggested that the effect of contouring workshops in terms of improving consistency amongst observers fades over time [53]. This points towards a need for continuous monitoring, evaluation, education and training. It is likely that automation and improvement in routine data collection can help in this evaluation, where each centre could continuously monitor their practice and correct any unexpected "drift" in the application of guidelines.

Any such use of automation, large-scale data collection and analysis or other machine learning and artificial intelligence applications in radiation oncology present challenges and pitfalls, as well as great opportunities [54,55]. Therefore, these developments themselves require careful evaluation, implementation, validation and QA before being applied in clinical practice. ESTRO activity, through the ESTRO Physics Research Workshops series, has led to guidelines on this and recommendations for a structured clinical data science community [56,57].

The role of ECG includes various strands: to develop and prioritize ESTRO clinical and technical guidelines; to consider ESTRO contributions to multidisciplinary guidelines with other oncology societies in Europe or more widely (e.g. ECCO, ASTRO, UICC), extending also to joint guidelines with relevant medical physics societies (e.g. AAPM, EFOMP) or other international bodies (e.g. IAEA, ICRU); to consider the potential impact of emerging legislation or advice, or other initiatives, on the strategic development of European Radiation Oncology; and to strategically assess other relevant documents, guidelines and information that may impact on clinical service development in Radiation Oncology. Thus, other ESTRO-based guidelines for structural, clinical and technical areas of the specialism have arisen from ACROP/EGC initiatives, as well as from other ESTRO activity, such as the research workshops. For example, ESTRO guidelines are an important instrument for the safe implementation of new radiotherapy techniques and technologies, respectively. Recent examples are MRI-guided radiotherapy using hybrid MRI-Linac units [58], surface guided radiotherapy [59,60], or the standardized qualitative assessment of treatment plans as pre-requisite for automated planning [61,62]. An example closely linked to the clinical delineation and treatment planning guidelines outlined above, is the RATING scoring guideline [63], providing structured approaches for considerations in designing, carrying out, evaluating and reporting comparative treatment planning studies. This has gradually become a widely accepted and used method to ensure and evaluate the quality of such studies. As such the ESTRO community, with its researchers and experts from leading radiation oncology institutions and early adopters of technology, provides guidance for the overall development and improvements in our field.

The ultimate goal of new techniques and technologies is to improve outcome and to provide clinical evidence. As one significant example, ESTRO has reacted to the increasing use of proton therapy in Europe by establishing its European Particle Therapy Network (EPTN). The EPTN has been very active in publishing clinical guidelines on contouring [64,65] taking into account the specific aspects of proton therapy, or in performing surveys as starting points for harmonization of procedures [66,67] including patient follow up [68]. Moreover, it fosters research collaboration and multicentric trials, i.e., key activities to bring proton therapy to the next level by concerted collaborative efforts [69,70].

Guidelines for new radiotherapy techniques today are in most aspects still expert opinions, thus providing a low level of evidence. They are nevertheless important to streamline the activities and the applications of new techniques and to ensure a homogeneous routine over as many countries and centres as possible. Notably, there are also guidelines on more established techniques or treatment guidelines on tumour entities. Here, high levels of evidence are supporting the statements in the guidelines. Within the coming years, we should come to a quality procedure that ensures that levels of evidence are given for each statement and recommendation in a guideline, including guidelines on treatment techniques.

Finally, to support the development of the multi-disciplinary staff groups in radiation oncology, ESTRO has a key role in providing education, training and the establishment of competencies to fulfill its mission and vision. Activity includes harmonization and standardization of education across Europe in the form of ESTRO's core curricula [29,71–75] and its wide range of training courses. Guidelines are widely used in the teaching courses and thus these in turn support the maintenance and evolution of high-quality clinical services, the development of radiation oncology practice as science, technology, knowledge and experience advance, and the underpinning of the development and implementation of further guidelines to encourage consistent clinical practice.

In summary, ESTRO clinical and other guidelines are soundly based, but always require validation, careful and consistent implementation, and focused education and training on their use, as well as local monitoring of that. As guidelines develop and older ones become superseded, there should be a clear mechanism to inform the community of the status of specific guidelines, especially when they have been replaced by new or updated versions. An important scientific aim for the future is to further advance guidelines and their individual statements into fully evidence-based instruments. These, in principle, could be directly linked to growing data-bases, allowing feedback mechanisms and thus continuous optimization. Another challenging research topic is the interplay of guidelines with growing opportunities and demands of personalized approaches of treatment.

Conflict of interest

All the authors have approved the final version. There is no conflict of interest in connection with this work and the material described is not under publication or consideration for publication elsewhere.

References

[1] Pötter R, Haie-Meder C, Van Limbergen E, Barillot I, De Brabandere M, Dimopoulos J, et al. Recommendations from gynaecological (GYN) GEC ESTRO working group (II): concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy-3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology. Radiother Oncol 2006;78:67–77. https://doi.org/10.1016/j.radonc.2005.11.014.

[2] Haie-Meder C, Pötter R, Van Limbergen E, Briot E, De Brabandere M, Dimopoulos J, et al. Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (I): concepts and terms in 3D image based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV. Radiother Oncol 2005;74:235–45. https://doi.org/10.1016/j.radonc.2004.12.015.

[3] Polgár C, Van Limbergen E, Pötter R, Kovács G, Polo A, Lyczek J, et al. Patient selection for accelerated partial-breast irradiation (APBI) after breast-conserving surgery: recommendations of the Groupe Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) breast cancer working group based on clinical evidence (2009). Radiother Oncol 2010;94:264–73. https://doi.org/10.1016/j.radonc.2010.01.014.

[4] Offersen BV, Boersma LJ, Kirkove C, Hol S, Aznar MC, Biete Sola A, et al. ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer. Radiother Oncol 2015;114:3–10. https://doi.org/10.1016/j.radonc.2014.11.030.

[5] Dimopoulos JC, Petrow P, Tanderup K, Petric P, Berger D, Kirisits C, et al. Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (IV): Basic principles and parameters for MR imaging within the frame of image based adaptive cervix cancer brachytherapy. Radiother Oncol 2012;103:113–22. https://doi.org/10.1016/j.radonc.2011.12.024.

[6] Ash D, Flynn A, Battermann J, de Reijke T, Lavagnini P, Blank L, et al. ESTRO/EAU/EORTC recommendations on permanent seed implantation for localized prostate cancer. Radiother Oncol 2000;57:315–21. https://doi.org/10.1016/s0167-8140(00)00306-6.

[7] Valentini V, Aristei C, Glimelius B, Minsky BD, Beets-Tan R, Borras JM, et al. Multidisciplinary Rectal Cancer Management: 2nd European Rectal Cancer

Consensus Conference (EURECA-CC2). Radiother Oncol 2009;92:148–63. https://doi.org/10.1016/j.radonc.2009.06.027.
[8] Cibula D, Pötter R, Planchamp F, Avall-Lundqvist E, Fischerova D, Haie Meder C, et al. The European Society of Gynaecological Oncology/European Society for Radiotherapy and Oncology/European Society of Pathology guidelines for the management of patients with cervical cancer. Radiother Oncol 2018;127:404–16. https://doi.org/10.1016/j.radonc.2018.03.003.
[9] Hellebust TP, Kirisits C, Berger D, Pérez-Calatayud J, De Brabandere M, De Leeuw A, et al. Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group: considerations and pitfalls in commissioning and applicator reconstruction in 3D image-based treatment planning of cervix cancer brachytherapy. Radiother Oncol 2010;96:153–60. https://doi.org/10.1016/j.radonc.2010.06.004.
[10] Salembier C, Lavagnini P, Nickers P, Mangili P, Rijnders A, Polo A, et al. Tumour and target volumes in permanent prostate brachytherapy: a supplement to the ESTRO/EAU/EORTC recommendations on prostate brachytherapy. Radiother Oncol 2007;83:3–10. https://doi.org/10.1016/j.radonc.2007.01.014.
[11] Niyazi M, Brada M, Chalmers AJ, Combs SE, Erridge SC, Fiorentino A, et al. ESTRO-ACROP guideline "target delineation of glioblastomas". Radiother Oncol 2016;118:35–42. https://doi.org/10.1016/j.radonc.2015.12.003.
[12] Hoskin PJ, Colombo A, Henry A, Niehoff P, Paulsen Hellebust T, et al. GEC/ESTRO recommendations on high dose rate afterloading brachytherapy for localised prostate cancer: an update. Radiother Oncol 2013;107:325–32. https://doi.org/10.1016/j.radonc.2013.05.002.
[13] Guckenberger M, Andratschke N, Dieckmann K, Hoogeman MS, Hoyer M, Hurkmans C, et al. ESTRO ACROP consensus guideline on implementation and practice of stereotactic body radiotherapy for peripherally located early stage non-small cell lung cancer. Radiother Oncol 2017;124:11–7. https://doi.org/10.1016/j.radonc.2017.05.012.
[14] Kovács G, Pötter R, Loch T, Hammer J, Kolkman-Deurloo IK, de la Rosette JJ, et al. GEC/ESTRO-EAU recommendations on temporary brachytherapy using stepping sources for localised prostate cancer. Radiother Oncol 2005;74:137–48. https://doi.org/10.1016/j.radonc.2004.09.004.
[15] Mazeron JJ, Ardiet JM, Haie-Méder C, Kovács G, Levendag P, Peiffert D, et al. GEC-ESTRO recommendations for brachytherapy for head and neck squamous cell carcinomas. Radiother Oncol 2009;91:150–6. https://doi.org/10.1016/j.radonc.2009.01.005.
[16] Korreman S, Rasch C, McNair H, Verellen D, Oelfke U, Maingon P, et al. The European Society of Therapeutic Radiology and Oncology-European Institute of Radiotherapy (ESTRO-EIR) report on 3D CT-based in-room image guidance systems: a practical and technical review and guide. Radiother Oncol 2010;94:129–44. https://doi.org/10.1016/j.radonc.2010.01.004.
[17] Glynne-Jones R, Nilsson PJ, Aschele C, Goh V, Peiffert D, Cervantes A, et al. Anal cancer: ESMO-ESSO-ESTRO clinical practice guidelines for diagnosis, treatment and follow-up. Radiother Oncol 2014;111:330–9. https://doi.org/10.1016/j.radonc.2014.04.013.
[18] Slotman BJ, Cottier B, Bentzen SM, Heeren G, Lievens Y, van den Bogaert W. Overview of national guidelines for infrastructure and staffing of radiotherapy. ESTRO-QUARTS: work package 1. Radiother Oncol 2005;75:349–54. https://doi.org/10.1016/j.radonc.2004.12.005.
[19] Colombo N, Creutzberg C, Amant F, Bosse T, González-Martín A, Ledermann J, et al. ESMO-ESGO-ESTRO consensus conference on endometrial cancer: Diagnosis, treatment and follow-up. Radiother Oncol 2015;117:559–81. https://doi.org/10.1016/j.radonc.2015.11.013.
[20] Offersen BV, Boersma LJ, Kirkove C, Hol S, Aznar MC, Sola AB, et al. ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer, version 1.1. Radiother Oncol 2016;118:205–8. https://doi.org/10.1016/j.radonc.2015.12.027.
[21] Grégoire V, Ang K, Budach W, Grau C, Hamoir M, Langendijk JA, et al. Delineation of the neck node levels for head and neck tumors: a 2013 update. DAHANCA, EORTC, HKNPCSG, NCIC CTG, NCRI, RTOG, TROG consensus guidelines. Radiother Oncol 2014;110:172–81. https://doi.org/10.1016/j.radonc.2013.10.010.
[22] Combs SE, Baumert BG, Bendszus M, Bozzao A, Brada M, Fariselli L, et al. ESTRO ACROP guideline for target volume delineation of skull base tumors. Radiother Oncol 2021;156:80–94. https://doi.org/10.1016/j.radonc.2020.11.014.
[23] Brouwer CL, Steenbakkers RJ, Bourhis J, Budach W, Grau C, Grégoire V, et al. CT-based delineation of organs at risk in the head and neck region: DAHANCA, EORTC, GORTEC, HKNPCSG, NCIC CTG, NCRI, NRG Oncology and TROG consensus guidelines. Radiother Oncol 2015;117:83–90. https://doi.org/10.1016/j.radonc.2015.07.041.
[24] Valentini V, Gambacorta MA, Barbaro B, Chiloiro G, Coco C, Das P, et al. International consensus guidelines on Clinical Target Volume delineation in rectal cancer. Radiother Oncol 2016;120:195–201. https://doi.org/10.1016/j.radonc.2016.07.017.
[25] Mir R, Kelly SM, Xiao Y, Moore A, Clark CH, Clementel E, et al. Organ at risk delineation for radiation therapy clinical trials: Global Harmonization Group consensus guidelines. Radiother Oncol 2020;150:30–9. https://doi.org/10.1016/j.radonc.2020.05.038.
[26] Lievens Y, Guckenberger M, Gomez D, Hoyer M, Iyengar P, Kindts I, et al. Defining oligometastatic disease from a radiation oncology perspective: An ESTRO-ASTRO consensus document. Radiother Oncol 2020;148:157–66. https://doi.org/10.1016/j.radonc.2020.04.003.
[27] Peters LJ, O'Sullivan B, Giralt J, Fitzgerald TJ, Trotti A, Bernier J, et al. Critical impact of radiotherapy protocol compliance and quality in the treatment of advanced head and neck cancer: results from TROG 02.02. J Clin Oncol 2010;28:2996–3001. https://doi.org/10.1200/JCO.2009.27.4498.
[28] Ohri N, Shen X, Dicker AP, Doyle LA, Harrison AS, Showalter TN. Radiotherapy Protocol Deviations and Clinical Outcomes: A Meta-analysis of Cooperative Group Clinical Trials. J Natl Cancer Inst 2013;105:387–93.
[29] Benstead K, Lara PC, Andreopoulos D, Bibault JE, Dix A, Eller YG, et al. Recommended ESTRO Core Curriculum for Radiation Oncology/Radiotherapy. Radiother Oncol 2019;141:1–4. https://doi.org/10.1016/j.radonc.2019.08.013.
[30] Eriksen JG, Leech M, Benstead K, Verfaillie C. Perspectives on medical education in radiation oncology and the role of the ESTRO School. Clin Transl Radiat Oncol 2016;1:15–8. https://doi.org/10.1016/j.ctro.2016.10.001.
[31] Bibault JE, Franco P, Borst GR, Van Elmpt W, Thorwhart D, Schmid MP, et al. Learning radiation oncology in Europe: Results of the ESTRO multidisciplinary survey. Clin Transl Radiat Oncol 2018;9:61–7. https://doi.org/10.1016/j.ctro.2018.02.001.
[32] Pötter R, Tanderup K, Schmid MP, Jürgenliemk-Schulz I, Haie-Meder C, Fokdal LU, et al. MRI-guided adaptive brachytherapy in locally advanced cervical cancer (EMBRACE-I): a multicentre prospective cohort study. Lancet Oncol 2021;22:538–47. https://doi.org/10.1016/S1470-2045(20)30753-1.
[33] Serban M, Kirisits C, Pötter R, de Leeuw A, Nkiwane K, Dumas I, et al. Isodose surface volumes in cervix cancer brachytherapy: Change of practice from standard (Point A) to individualized image guided adaptive (EMBRACE I) brachytherapy. Radiother Oncol 2018;129:567–74. https://doi.org/10.1016/j.radonc.2018.09.002.
[34] Jensen NBK, Pötter R, Kirchheiner K, Fokdal L, Lindegaard JC, Kirisits C, et al. Bowel morbidity following radiochemotherapy and image-guided adaptive brachytherapy for cervical cancer: Physician- and patient reported outcome from the EMBRACE study. Radiother Oncol 2018;127:431–9. https://doi.org/10.1016/j.radonc.2018.05.016.
[35] Fokdal L, Pötter R, Kirchheiner K, Lindegaard JC, Jensen NBK, Kirisits C, et al. Physician assessed and patient reported urinary morbidity after radiochemotherapy and image guided adaptive brachytherapy for locally advanced cervical cancer. Radiother Oncol 2018;127:423–30. https://doi.org/10.1016/j.radonc.2018.05.002.
[36] Najjari Jamal D, Pötter R, Haie-Meder C, Lindegaard JC, Juergenliemk-Schulz IM, Mahantshetty U, et al. Physician assessed and patient reported lower limb edema after definitive radio(chemo)therapy and image-guided adaptive brachytherapy for locally advanced cervical cancer: A report from the EMBRACE study. Radiother Oncol 2018;127:449–55. https://doi.org/10.1016/j.radonc.2018.03.026.
[37] Smet S, Pötter R, Haie-Meder C, Lindegaard JC, Schulz-Juergenliemk I, Mahantshetty U, et al. Fatigue, insomnia and hot flashes after definitive radiochemotherapy and image-guided adaptive brachytherapy for locally advanced cervical cancer: An analysis from the EMBRACE study. Radiother Oncol 2018;127:440–8. https://doi.org/10.1016/j.radonc.2018.03.009.
[38] Pötter R, Tanderup K, Kirisits C, de Leeuw A, Kirchheiner K, Nout R, et al. The EMBRACE II study: The outcome and prospect of two decades of evolution within the GEC-ESTRO GYN working group and the EMBRACE studies. Clin Transl Radiat Oncol 2018;9:48–60. https://doi.org/10.1016/j.ctro.2018.01.001.
[39] Bell JA, Balneaves LG. Cancer patient decision making related to clinical trial participation: an integrative review with implications for patients' relational autonomy. Support Care Cancer 2015;23:1169–96. https://doi.org/10.1007/s00520-014-2581-9.
[40] Field M, Vinod S, Aherne N, Carolan M, Dekker A, Delaney G, et al. Implementation of the Australian Computer Assisted Theragnostics (AusCAT) network for radiation oncology data extraction, reporting and distributed learning. J Med Imag Radiat Oncol 2021;65:627–36. https://doi.org/10.1111/1754-9485.13287.
[41] Barazzuol L, Coppes RP, van Luijk P. Prevention and treatment of radiotherapy-induced side effects. Mol Oncol 2020;14:1538–54.
[42] Baumann M, Krause M, Overgaard J, Debus J, Bentzen SM, Daartz J, et al. Radiation oncology in the era of precision medicine. Nat Rev Cancer 2016;16:234–49.
[43] Lambin P, Leijenaar RTH, Deist TM, et al. Radiomics: the bridge between medical imaging and personalized medicine. Nat Rev Clin Oncol 2017;14:749–62.
[44] Bodalal Z, Trebeschi S, Nguyen-Kim TDL, et al. Radiogenomics: bridging imaging and genomics. Abdom Radiol 2019;44:1960–84.
[45] Wee L, van Kuijk SMJ, Dankers FJWM, Traverso A, Welch M, Dekker A. Reporting standards and critical appraisal of prediction models. In: Kubben P, Dumontier M, Dekker A, editors. Fundamentals of clinical data science. Cham: Springer; 2019.
[46] Collins GS, Reitsma JB, Altman DG, Moons KGM. Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD): the TRIPOD statement. Ann Intern Med 2015;162:55.
[47] Moons KGM, Altman DG, Reitsma JB, Ioannidis JPA, Macaskill P, Steyerberg EW, et al. Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD): Explanation and Elaboration. Ann Intern Med 2015;162:W1.
[48] Zwanenburg, Vallières, Abdalah et al. The image biomarker standardization initiative: standardized quantitative radiomics for high-throughput image-based phenotyping. Radiology 220;295:328-338
[49] Zwanenburg A, Löck S. Why validation of prognostic models matters? Radiother Oncol 2018;127:370–3.
[50] Dutz A, Löck S. Competing risks in survival data analysis. Radiother Oncol 2019;130:185–9.

[51] Eriksen JG, Salembier C, Rivera S, De Bari B, Berger D, Mantello G, et al. Four years with FALCON – An ESTRO educational project: Achievements and perspectives. Radiother Oncol 2014;112:145–9. https://doi.org/10.1016/j.radonc.2014.06.017.
[52] De Bari B, Dahele M, Palmu M, Kaylor S, Schiappacasse L, Guckenberger M. Short interactive workshops reduce variability in contouring treatment volumes for spine stereotactic body radiation therapy: Experience with the ESTRO FALCON programme and EduCase™ training tool. Radiother Oncol 2018;127:150–3. https://doi.org/10.1016/j.radonc.2017.10.038.
[53] Mercieca S, Belderbos JSA, van Baardwijk A, Delorme S, van Herk M. The impact of training and professional collaboration on the interobserver variation of lung cancer delineations: a multi-institutional study. Acta Oncol 2019;58:200–8. https://doi.org/10.1080/0284186X.2018.1529422.
[54] Thompson RF, Valdes G, Fuller CD, Carpenter CM, Morin O, Aneja S, et al. Artificial intelligence in radiation oncology: a specialty-wide disruptive transformation? Radiother Oncol 2018;129:421–6. https://doi.org/10.1016/j.radonc.2018.05.030.
[55] Thwaites DI, Moses D, Haworth A, Barton M, Holloway L. Artificial Intelligence in Medical Imaging and Radiation Oncology: Opportunities and Challenges. J Med Imag Rad Onc 2021;65:481–5. https://doi.org/10.1111/1754-9485.13275.
[56] Vandewinckele L, Claessens M, Dinkla A, Brouwer C, Crijns W, Verellen D, et al. Overview of artificial intelligence-based applications in radiotherapy: Recommendations for implementation and quality assurance. Radiother Oncol 2020;153:55–66. https://doi.org/10.1016/j.radonc.2020.09.008.
[57] Kazmierska J, Hope A, Spezi E, Beddar S, Nailon WH, Osong B, et al. From multisource data to clinical decision aids in radiation oncology: the need for a clinical data science community. Radiother Oncol 2020;153:43–54. https://doi.org/10.1016/j.radonc.2020.09.054.
[58] Corradini S, Alongi F, Andratschke N, Azria D, Bohoudi O, Boldrini L, et al. ESTRO-ACROP recommendations on the clinical implementation of hybrid MR-linac systems in radiation oncology. Radiother Oncol 2021;159:146–54. https://doi.org/10.1016/j.radonc.2021.03.025.
[59] Freislederer P, Batista V, Öllers M, Buschmann M, Steiner E, Kügele M, et al. ESTRO-ACROP guideline on surface guided radiation therapy. Radiother Oncol 2022;173:188–96. https://doi.org/10.1016/j.radonc.2022.05.026.
[60] Batista V, Meyer J, Kügele M, Al-Hallaq H. Clinical paradigms and challenges in surface guided radiation therapy: Where do we go from here? Radiother Oncol 2020;153:34–42. https://doi.org/10.1016/j.radonc.2020.09.041.
[61] Hernandez V, Hansen CR, Widesott L, Bäck A, Canters R, Fusella M, et al. What is plan quality in radiotherapy? The importance of evaluating dose metrics, complexity, and robustness of treatment plans. Radiother Oncol 2020;153:26–33. https://doi.org/10.1016/j.radonc.2020.09.038.
[62] Kaplan LP, Placidi L, Bäck A, Canters R, Hussein M, Vaniqui A, et al. Plan quality assessment in clinical practice: Results of the 2020 ESTRO survey on plan complexity and robustness. Radiother Oncol 2022;173:254–61. https://doi.org/10.1016/j.radonc.2022.06.005.
[63] Hansen CR, Crijns W, Hussein M, Rossi L, Gallego P, Verbakel W, et al. Radiotherapy Treatment plannINg study Guidelines (RATING): A framework for setting up and reporting on scientific treatment planning studies. Radiother Oncol 2020;153:67–78. https://doi.org/10.1016/j.radonc.2020.09.033.
[64] Crouzen JA, Petoukhova AL, Wiggenraad RGJ, Hutschemaekers S, Gadellaa-van Hooijdonk CGM, et al. Development and evaluation of an automated EPTN-consensus based organ at risk atlas in the brain on MRI. Radiother Oncol 2022;173:262–8. https://doi.org/10.1016/j.radonc.2022.06.004.
[65] Eekers DBP, Di Perri D, Roelofs E, Postma A, Dijkstra J, Ajithkumar T, et al. Update of the EPTN atlas for CT- and MR- based contouring in Neuro-Oncology. Radiother Oncol 2021;160:259–65. https://doi.org/10.1016/j.radonc.2021.05.013.
[66] Bolsi A, Peroni M, Amelio D, Dasu A, Stock M, Toma-Dasu I, et al. Practice patterns of image guided particle therapy in Europe: A 2016 survey of the European Particle Therapy Network (EPTN). Radiother Oncol 2018;128:4–8. https://doi.org/10.1016/j.radonc.2018.03.017.
[67] Knopf AC, Czerska K, Fracchiolla F, Graeff C, Molinelli S, Rinaldi I, et al. Clinical necessity of multi-image based optimization for targets affected by respiratory motion and treated with scanned particle therapy – A comprehensive review. Radiother Oncol 2022;169:77–85. https://doi.org/10.1016/j.radonc.2022.02.018.
[68] De Roeck L, van der Weide HL, Eekers DBP, Kramer MC, Alapetite C, Blomstrand M, et al. work package 1 of the taskforce "European Particle Therapy Network" of ESTRO. The European Particle Therapy Network (EPTN) consensus on the follow-up of adult patients with brain and skull base tumours treated with photon or proton irradiation. Radiother Oncol 2022;168:241–9. https://doi.org/10.1016/j.radonc.2022.01.018.
[69] Langendijk JA, Orecchia R, Haustermans K, Zips D, Balosso J, Lacombe D, et al. Prospective data registration and clinical trials for particle therapy in Europe. Radiother Oncol 2018;128:9–13. https://doi.org/10.1016/j.radonc.2018.06.001.
[70] Sørensen BS, Pawelke J, Bauer J, Burnet NG, Dasu A, Høyer M, et al. Does the uncertainty in relative biological effectiveness affect patient treatment in proton therapy? Radiother Oncol 2021;163:177–84. https://doi.org/10.1016/j.radonc.2021.08.016.
[71] Benstead K, Lara PC, Eller Y, Engell-Noerregaard L, Eriksen JG, Gaye PM, et al. Clinical oncology module for the ESTRO core curriculum. Radiother Oncol 2021;156:19–22. https://doi.org/10.1016/j.radonc.2020.11.029.
[72] Fiorino C, Jeraj R, Clark CH, Garibaldi C, Georg D, Muren L, et al. Grand challenges for medical physics in radiation oncology. Radiother Oncol 2020;153:7–14. https://doi.org/10.1016/j.radonc.2020.10.001.
[73] Garibaldi C, Essers M, Heijmen B, Bertholet J, Koutsouveli E, Schwarz M, et al. The 3rdESTRO-EFOMP core curriculum for medical physics experts in radiotherapy. Radiother Oncol 2022;170:89–94. https://doi.org/10.1016/j.radonc.2022.02.012.
[74] Coffey M, Leech M, Poortmans P. ESTRO RTT Committee. Benchmarking Radiation TherapisT (RTT) education for safe practice: The time is now. Radiother Oncol 2016;119:12–3. https://doi.org/10.1016/j.radonc.2016.03.008.
[75] Coffey M, Leech M. ESTRO Radiation TherapisT Committee. The European Society of Radiotherapy and Oncology (ESTRO) European Higher Education Area levels 7 and 8 postgraduate benchmarking document for Radiation TherapisTs (RTTs). Tech Innov Patient Support Radiat Oncol 2018;8:22–40. https://doi.org/10.1016/j.tipsro.2018.09.009.