ESTRO 2022: innovations in brachytherapy

ESTRO 2022 started on 6 May and came to a wonderful end on 10 May, 2022, in Copenhagen, Denmark. It was exciting to return to an on-site event to share recent work, research, and experiences with colleagues and friends. This year's meeting of the European SocieTy for Radiotherapy and Oncology (ESTRO) involved enriching presentations that encompassed all radiation oncology research and clinical domains. The brachytherapy track made a vast and compelling contribution. Here we summarise some of the innovations in brachytherapy and future development paths for this treatment modality, as we perceive them from presentations at ESTRO 2022.

Teaching lecture and debate

The track opened with a teaching lecture by Dr Henrike Westerveld entitled "Improving radiotherapy outcome for vaginal tumours using a joint target concept". It discussed the prominent role of brachytherapy in vaginal cancer treatment and the position of MRI as the best imaging method for visualisation of such tumours. High doses (>80Gy) have been shown to lead to improvement of local control in advanced tumours (T2-4), but there is still room to improve pelvic control in advanced stages and to decrease rates of severe late morbidity. Validation of ways in which to achieve this, through the performance of a large prospective study that involves a common language for contouring and reporting, is necessary.

The lecture was followed by a debate on the different treatment approaches for soft tissue sarcomas. External beam and intra-operative radiation therapies (EBRT and IORT) and brachytherapy radiation modalities, or combinations of them, were evaluated. Based on current clinical practice, Dr Marta Gimeno Morales presented brachytherapy as a versatile technique that could be used as a monotherapy for high- and intermediate-grade, small, primary tumours. For larger tumours or positive margins after surgery, brachytherapy could be used to boost EBRT. During the session discussion, the questions were geared towards concerns regarding the combination of radiation modalities and the evaluation of radiobiological outputs. In conclusion, there is a need for research in brachytherapy to validate the use of the equivalent dose in 2Gy fractions (EQD2) during use of brachytherapy or IORT with conventional external beam therapy.

Brachytherapy physics

The first half of the presentations in the brachytherapy physics session described advances towards improved in-vivo dosimetry. The session started with the Groupe Européen de Curiethérapie (GEC)-ESTRO best junior presentation, which was entitled: "Brachytherapy treatment verification using a moving phantom" and was presented by Dr TP van Wagenberg. This work explores the use of a realistic model to evaluate the impact of motion-related errors on treatment parameters (dwell time and position) through the use of a moving phantom. The parameters were obtained with similar accuracy as for a static phantom, and the use of a 3D camera enabled the distinguishing of internal (source) and external (phantom) motion.

The next talk, by Dr Eric Brost, presented the improvements that could be obtained in ultrasound visibility of high-dose-rate (HDR) brachytherapy catheters through the use of a commercial echogenic coating. The coated surface reduced reverberation artifacts and improved the needle visibility when brachytherapy needles were implanted at an angle to the ultrasound probe or in the presence of B-mode signal degradation.

The session was followed by one by Vaiva Kaveckyte, whose work exploits advantageous properties of high-atomic-number inorganic scintillators over the more common organic versions for Ir192 in-vivo dosimetry, such as greater light output and negligible stem-effect. The larger absorbed-dose energy dependence of high-Z scintillators, among other dosimetry challenges, was studied through the use of Monte Carlo simulation, and the alternative detectors were characterised.

The presentation by Professor Jacob G. Johansen introduced an online verification system that could enable rectification in real-time brachytherapy through the comparison of measured doses with the expected, pre-calculated values from the treatment planning system (TPS). The method could be implemented easily in the clinic and adds no more than 20 minutes to workload.

Continuing with innovations in brachytherapy dosimetry, Dr Sarah Wilby presented the first study of micro-silica thermoluminescent dosimeters that had been characterised for use with low energy photons (27keV) of I125 seeds. Beads have the potential to be valuable dosimeters in brachytherapy due to their small size, which enables high spatial resolution.

The session concluded with work by Dr Thorsten Schneider on electronic brachytherapy. The use of electronic brachytherapy sources such as the INTRABEAM is increasing. The dosimetry of the system is provided by the manufacturer in the form of dose

and depth-dose distribution for the bare needle configuration, which can be converted to dose from the applicator configuration through the use of an applicator-transfer function. Dr Schneider presented advances towards the absolute dosimetry of the bare-needle system, which had been made at the PTB primary standards laboratory.

Proffered papers: physics, gynaecology and prostate

This session was begun by Dr Tibor Major, who had investigated the dosimetric differences that had been exhibited in studies of brachytherapy compared with EBRT. In terms of dose to organs-at-risk (OARs), brachytherapy performed better or as well as the most advanced EBRT techniques in most of the studies that were considered. The conclusion was that brachytherapy had a clear future in cancer treatment.

The next presentation, by Frida Dohlmar, described an in-house adjustment tool that had been developed to improve automated clinical-treatment plans for brachytherapy, especially in terms of dose homogeneity. Automated plans may present advantages over manual versions as they can be produced more quickly and are less dependent on the planner's skills, and thus the tool can benefit the brachytherapy workflow and outcomes.

In the same trend, Anton Bouter presented a method to improve dose distributions in prostate plans through the use of the BRIGHT automated treatment-planning tool. The method involved minimisation of contiguous high-dose volumes (hotspots) while minimally impacting the dose-volume indices (DVIs).

The talk by Ioannis Androulakis explained the exploitation of the thermally enhanced radiation sensitivity of tumours by combining thermotherapy with brachytherapy in a technique called thermobrachytherapy. The researchers developed a method to deliver both techniques simultaneously to optimise outcomes. The results showed a decreased dose to OARs while maintaining a similar EQD to the target.

Work presented by Robin Straathof has cleverly explored, for the first time, the influence of flexible brachytherapy instruments on the source paths and the insertion forces of catheters in curved applicator channels. As a result, novel 3D-printed brachytherapy applicators can be developed and the accuracy of source-path models in current applicator libraries can be improved.

The session concluded with a talk by Dr Inger-Karine Kolkman-Deurloo, who demonstrated the feasibility of a hybrid electromagnetic tracking brachytherapy system that detects positional treatment errors and reconstruction uncertainties in cervical cancer patients who undergo HDR brachytherapy.

Artificial intelligence and brachytherapy

The teaching lecture entitled "Artificial intelligence and brachytherapy: current reality and perspectives" was presented from the perspectives of a radiation oncologist (Dr Luca Tagliaferri) and a medical physicist (Dr Nicole Nesvacil). Dr Tagliaferri described, from a patient-centric point of view, how artificial intelligence (AI) could aid the radiation oncology brachytherapy clinical workflow. From the first patient consultation through implant, delineation, planning and treatment session delivery, to decision support for an adjuvant approach at the end of treatment, he considered aspects such as the provision of clinical decision support; mining-omics and analysis of data; radiomics and genomics; facilitation of repetitive tasks and optimisation of time; and modelling behaviours, in a heterogeneous context. Big-data analysis and AI can provide significant advantages for physicians as tools that enable more time to be dedicated to physician-patient interaction. This then impacts clinical oncological practice and the interventional radiotherapy workflow. This includes clinical-outcome improvements (predictive models and decision support system); quality assurance improvement (automatic error detection system); reduction in cure costs (automation); and escape from time-consuming repetitive tasks (advantages in contouring and delivery). Subsequently, Dr Nesvacil presented a thorough and comprehensive view of the current status of the implementation of brachytherapy automation in TPSs, which ranged from implant planning (pre-planning) through targets and OAR contouring, applicator reconstruction, dose-distribution optimisation, plan evaluation and the making of clinical decisions for best option by comparing prescribed dose and planning aim. Validation of AI algorithms for predictive modelling and contouring in a multi-centre context to ensure model generalisability and transferability is essential. To this end, Dr Tagliaferri highlighted the consortium for brachytherapy data analysis project, in which a large multicentre database was created to validate predictive models externally. This talk illustrated the need for standardised data collection that implemented distributed learning approaches in data sharing and inspired the transparency of in-house modelling algorithms for external reproducibility and use. By working together, we will be able to achieve clinical translation of AI algorithms from research to practice.

Symposium on the use of imaging in prostate brachytherapy

A symposium on the use of imaging in prostate brachytherapy followed the AI symposium. First, Dr Gerard Morton described the imaging modalities for target definition. A comprehensive HDR brachytherapy programme requires quality imaging that may include modern ultrasound, MRI and access to molecular imaging. Multiparametric MRI and positron-emission tomography that uses prostate-specific membrane antigens provide the best available local staging information. This talk was followed by one by Professor Frank-André Siebert, in which he described state-of-the-art image registration in computer-tomography-based,

ultrasound-based, HDR brachytherapy of the prostate. Prospective contributions from AI-based models to the development of image registration are emerging but uncertainties remain high.

Dr Simon Buus closed the session with a demonstration of the feasibility of real-time, MRI-based, HDR brachytherapy of the prostate. Compared with commonly used transrectal ultrasound scans (TRUS), MRI provides an improved definition of the target and OARs and improved catheter placement and definition, and online treatment can be verified.

Gynaecology

The gynaecology session started with a presentation from Dr Angeles Rovirosa entitled "3D image-guided brachytherapy plus irradiation in stages-I-III inoperable endometrial cancer". She concluded that in this type of cancer, the use of image-guided brachytherapy (IGBT) with EBRT offered good cancer-specific survival results of 88.7% and 71.2% after two and five years, respectively. The best outcomes were achieved in stages I and II. 3D-IGBT provides effective treatment for inoperable cancers and prospective studies should help to determine how better outcomes can be obtained.

A unique study by Sharline van Vliet-Perez presented data on "Patient experience and time-action analysis during cervical cancer brachytherapy". The researchers encouraged other brachytherapy researchers to identify gaps in current clinical practice and innovations that would enhance patient experiences via automation. They reported that pain and anxiety scores were found to be highest during the waiting period before treatment and during applicator removal, although there were large inter- and intra-patient variations. In future, the time-action and patient-experience analysis could be used to optimise various steps in brachytherapy delivery.

Treatment planning automation studies with bi-objective and multi-objective approaches for brachytherapy treatment of cervical cancer were presented by Leah R.M. Dickhoff and Rik Bijman, respectively. The former (bi-objective) was an automated approach, which enabled an efficient generation of clinically acceptable treatment plans with DVI optimisation. The least coverage and least sparing indices were the two objectives of the optimisation models. Trade-offs between target coverage and organ sparing were realised through optimisation of this model, which gave rise to a set of treatment plans. The researchers found that the direct extension of this bi-objective optimisation approach from prostate HDR brachytherapy, which worked well, to cervical cancer with the use of only the protocol from the image-guided intensity-modulated external-beam radiochemotherapy and MRI-based adaptive brachytherapy in locally advanced cervical cancer (EMBRACE-II) study required additional planning aims to achieve desirable plans.

The researchers in the multi-objective study aimed to satisfy not only targets and OAR requirements, but also non-dosimetric objectives for the prevention of high-dwell-time gradients and unbalanced intracavitary, ovoid, and interstitial needle usage. Consequently, they implemented successfully fully automated, adaptive, multi-criteria planning for brachytherapy treatment of cervical cancer with improved efficiency in planning time (<2 minutes) and improved plan quality (i.e. autoplanning achieved lower OAR EQD2 when compared with clinical planning for similar coverage of high-risk clinical-target volumes (CTVs)).

Dr Laura Allex's team explained their exploration and testing of a clinical QA (cQA) system for image-guided adaptive brachytherapy in the context of chemo-radiation for cervical cancer patients. Seventeen key performance indicators and a minimal required set of six dose-volume checkpoints for patient-specific cQA were established, leading to a feasible cQA system for implementation in routine clinical practice. Peter Georgi then gave a stimulating talk entitled "Scintillator-based in-vivo dosimetry during pulsed-dose-rate brachytherapy for cervical cancer". The researcher was motivated by documented incidents of dose misadministration due to treatment planning errors, applicator misplacements and registration errors, anatomical motion and equipment malfunctions. In the study, he aimed to measure dose rate during pulsed-dose-rate brachytherapy for gynaecological cancers and characterise inter-pulse and inter-dwell-time dosimetric stability, and to validate treatment. They achieved this through the use of adaptive time-resolved in-vivo dosimetry with a scintillator-based detector system that had been developed in-house. They showed that the accumulated dose per pulse was within 10% of expectations in pulsed-dose-rate brachytherapy treatments. They explored this deviation through the use of time-resolved dosimetry, and discovered inconsistencies between planned and actual dwell positions, which explained the deviation.

Brachytherapy best paper

The best brachytherapy paper award went to Dr Monica Serban. Her research analysed the effect of dose de-escalation and compressed EBRT and brachytherapy fractionation schedules on target and organ doses in low-risk cervical cancer. The researchers showed that an EBRT dose of 40Gy/20fractions together with a response-adaptive brachytherapy dose prescription of 85Gy or 90Gy EQD210 would significantly reduce hotspot doses in OARs by 2-6Gy with clinical brachytherapy schedules, or by 0-4Gy with shorter schedules. Consequently, bowel, bladder and rectum volumes that received more than 15Gy, 30Gy and 40Gy (V15Gy, V30Gy, and V40Gy) were considerably reduced, by 15-60%. Substantial reduction of G2 and G3 toxicity was expected, which would lead to reductions in the number of necessary fractions and diminished treatment burdens. The EMBRACE III study will take a risk-stratified approach adapted to individual patients. It is set to begin in 2023, and will involve testing these fractionation schedules in a prospective, phase 2 study (EMBRACE III low-risk protocol).

A session on ocular plaque brachytherapy started with the description of I125 and Ru106 brachytherapy treatment planning and QA aspects by Dr Marisol De Brabandere. Dr De Brabandere emphasised the limitations of standardised methods for source calibration, applicator commissioning and treatment planning for the Ru106 source.

Lotte Stubkjær Fog then presented the results of a GEC-ESTRO survey that had been conducted on global Ru106 eye-plaque brachytherapy practice. The study has been well received and has revealed room for practice improvement in both the physics and clinical aspects.

Dr Bruno Fionda concluded the session with the topic: "Clinical management and treatment outcomes of eye plaque treatment of uveal melanoma". There is a lack of consensus on how uveal melanoma response should be assessed after brachytherapy. Dr Fionda showed the latest available evidence regarding its radiological and clinical assessment.

ESTRO-Elekta Brachytherapy award

The session "prostate, head & neck (H&N), eye" opened with the ESTRO-Elekta Brachytherapy award, which was given to Dr Ignacio Visus, who showed that HDR brachytherapy boosts improve metastatic and biochemical relapse-free survival rates, as compared with the use of EBRT alone, in high-risk prostate-cancer patients. Dr Max Peters showed that patients with recurrence of local prostate cancer could benefit from focal salvage HDR brachytherapy, with a decreased risk of late toxicity.

The next talk, by Sofia Garcia, revealed the role of the neutrophil-to-lymphocyte ratio (NLR) as a prognostic factor in low- to intermediate-risk prostate-cancer patients who were treated with I125 brachytherapy. High NLR was a strong predictor of worse overall survival, but no association was found between NLR and disease-free survival or disease-specific survival rates.

The next presentation, by Dr Artur Chyrek, showed that HDR brachytherapy was a highly effective treatment method for both primary and recurrent basal-cell carcinoma after standard surgical excision of the H&N region. Similarly, Dr Zoltán Takácsi-Nagy showed that treatment of tongue cancer with interstitial HDR brachytherapy after surgery resulted in slightly more favourable local control than did surgery or brachytherapy alone.

Mercedes González Cantero closed the session with a presentation of outcomes after brachytherapy in choroidal melanoma. She concluded that episcleral-plaque brachytherapy achieved good results in eyeball conservation and visual function preservation, with high rates of local-tumour control and progression-free survival.

Breast, rectum session

The breast and rectum session of proffered papers began with Judyta Wiercinska's presentation on "The use of hyaluronic acid hydrogel as a tumour bed marker in breast cancer brachytherapy". The researchers were motivated by evidence that localisation of a tumour bed and target volume definition were the sources of the greatest uncertainties in breast radiotherapy. They showed that the use of hydrogels based on hyaluronic acid as tumour-bed markers, reduced inter- and intra-observer variability of target volume delineation during brachytherapy boost.

Dr. Philippe Boissard's team provided evidence that 3D virtual brachytherapy using AlignRT may offer an improved technique to perform interstitial implants of the breast accurately in selected patients.

A variety of AI methods have been explored for brachytherapy applicator reconstruction; electromagnetic tracking (EMT) was used for automation of catheter reconstruction in interstitial breast brachytherapy, as described in the work of Christopher Durrbec. EMT is readily integrated into the clinical workflow and therefore has large potential to streamline interstitial brachytherapy implant reconstruction. Even though minor manual adjustments of reconstruction are needed to achieve the required doses, EMT remains a promising tool in the drive to make applicator reconstruction more time-efficient. This step consumes the most time in treatment planning.

Dr Rahul Krishnatry (presenting for Dr Reena Engineer) reported on endorectal brachytherapy, which is a safe and feasible technique to enhance complete response, reduce local regrowth and thus improve organ preservation in patients with distal rectal cancers. Dr Johan E. Van Limbergen made a case for dose and volume reporting for endorectal contact radiation boosts. Dose reporting and prescription to gross target volume, CTV and OARs on repeated imaging would provide insight regarding delivered dose, local control and toxicity to enable optimisation of treatment protocols.

Debate: This house believes that brachytherapy is a dying art

A debate entitled "This house believes that brachytherapy is a dying art" caught the attention of many. Bernd Wisgrill was against this proposition. He provided sound evidence such as the number of brachytherapy publications has increased; brachytherapy offers the dosimetric advantages of supplying a very large dose to the tumour while decreasing doses to OARs; shorter treatment time (fewer fractions) than required in other methods; brachytherapy is the standard-of-care in treatment of locally advanced cervical carcinoma, and can be used at all stages of the tumour when IGBT is used. New technologies in brachytherapy are being clinically evaluated, such as new applicators for gynae- and rectal brachytherapy that are MRI-compatible and can be rotated;

increasing use of AI and deep-learning in brachytherapy for image enhancement, image registration, CTV and OAR segmentation, applicator reconstruction and seed identification; image guidance using MRI and 3D-TRUS; new 3D-printing of applicators and personalised immobilisation gadgets; and increased use of virtual reality for personalised planning and training. By the end of this debate, 80% of the house voted that brachytherapy was not a dying art.

However, the shortcomings that brachytherapy faces should not be ignored. There is a need to train more brachytherapy practitioners. To attract and retain our brachytherapy talent, more education and training sites are required, and funding for brachytherapy research and education must be increased. This led into the symposium “Preserving brachytherapy skills for the future”, in which speakers shed light on the status of brachytherapy education and future requirements in Europe and North America.

Dr Christian Kirisits advocated the integration of brachytherapy into core curricula or the introduction of specialised brachytherapy physics education and certification to make the subject an integral part of continuous education and training. Dr Alina Sturdza summarised future initiatives as follows: advertise brachytherapy at the medical-student level and offer radiation oncology electives and courses, and in the media through patient-driven groups and cancer-aid societies; develop and implement a formal and comprehensive brachytherapy curriculum and log book that requires hands-on experience: increase the number of brachytherapy preparatory courses; and increase the use of simulation-based medical education.

Dr Mitchell Kamrava pointed out that despite the “cons'' in brachytherapy, such as low reimbursement (which can be improved by better funding models) and time-intensiveness (which can be significantly aided by AI applications), the “pros'' are indisputable. That is, brachytherapy “wins” in gynaecological cancer cases in terms of better local control, overall survival rates and lower toxicity compared with EBRT. Although less robust data is available for prostate and breast cancer treatment compared with gynaecological cancers, quality-of-life advantages are a strong driver of increased funding and education resources. Brachytherapists from around the world must adapt and build together.

General comments

The innovations in brachytherapy that were presented at ESTRO 2022 were nothing short of stimulating and inspiring for the future of this longstanding treatment modality. We have summarised exciting findings that were discussed in debates, teaching lectures and proffered papers. They included topics from current and future perspectives of AI in brachytherapy, to creative and illuminating results in brachytherapy physics, imaging methodology and technology in gynaecological, breast, rectum, prostate, H&N, and eye cancers, soft-tissue sarcoma and ocular-plaque brachytherapy. The discussions demonstrated the strength of brachytherapy. In the future, there must be more educational opportunities in brachytherapy to attract and retain trainees, more training sites, and more funding to support the development and translation of tangible research ideas into clinical practice. Brachytherapy is not a dying art, but a thriving one.

Yujing Zou
Medical Physics Unit
Department of Oncology
Faculty of Medicine
McGill University
Montreal, Canada

David Santiago Ayala Alvarez
Medical Physics Unit
Department of Physics
McGill University
Montreal, Canada