ESTRO 37

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CONGRESS REPORT

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ESTRO
European Society for
RADIOTHERAPY
& ONCOLOGY

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INTRODUCTION

YOLANDE LIEVENS

We imagine that ESTRO 37 was a great event. What were, in your view, the reasons for this success?
I believe it was first and foremost thanks to the large number of diverse topics that were addressed by the scientific programme committee, and brought forward by an huge group of enthusiastic speakers, both in the multidisciplinary and specific tracks. In addition to that, the clever harmonization of innovation and guidance for daily practice, a blend of cutting edge science with a review of the more standard-care approach, brings a combination that is of interest to a lot of attendees.

We had participation from all types of radiation oncology professionals, as well as from experts out of our field, coming from all over the world. This not only generated interesting scientific input, but also a fascinating interaction between different viewpoints from various regions of the globe.

Finally, we had around 2500 abstracts this year. The most we have ever had so far. This shows that people have an interest to be actively involved in our conference. In addition to acquiring knowledge from others, they like to interact and share their own experiences. I believe this aspect is extremely important in making the annual conference successful and our members involved in the Society.

On what did the sessions focus? Give a few examples
As mentioned before, the topics were broad and covering all aspects across the entire landscape of radiation oncology disciplines. Naming a few means ignoring so many others, which is not really what I want to do. It is important to mention, though, that we had highlighted throughout the conference programme those sessions that emphasised the conference theme: Innovation for Value and Access. With this theme, we wanted to highlight that our innovations in radiation therapy - all or not in combination with other oncology treatments - not only provide better outcome to our patients, but also allow us to provide these benefits to an ever-larger share of the cancer patient population. Not less than 26 sessions were in some way related to our conference theme, which I think really underscores the value of our treatments and profession!

Lastly, I would also like to mention that this year we used a different format for the opening ceremony. Instead of having a speaker out of the field of medicine, we now attracted a key-note speaker, Prof Rifat Atun from Harvard. Although trained as clinician, his career and research focus has been on the design and implementation of health systems reforms and their impact on outcomes. With his lecture entitled: "Health Systems, Innovation and Value Based Healthcare", he provided us with a wider scope to the work we do as radiation oncology professionals and a perfect introduction to our conference theme.

Has the scientific programme been developed to reflect the ESTRO vision? What about the newly proposed vision?
Yes, it was. The scientific programme of the conference was centred on our vision which states that European patients must have proper access to state of the art radiotherapy.

The programme reflected both the old ESTRO vision as well as the newly established one. The new vision statement is indeed a broader formulation of the main aspects belonging to ESTRO's former vision: in a nutshell, together we will bring the optimal treatment to all of our patients.

In what way was the congress an asset to professionals in radiation oncology? What did it bring to their knowledge and practice?
Every year we bring different nuances to the various sessions: we have the premeeting courses where professionals can choose a topic and get an in-depth overview and discussion of the specific subject. Then we have the symposia where the speakers – all experts on a theme – are sharing their knowledge with the audience, and, in case of the debates, provide lively discussion on the pros and cons of less clear-cut topics. Finally, we have the presentations from professionals themselves, from oral presentations to the different types of posters, bringing their own work and providing them the opportunity to discuss their experience with their peers.

As mentioned before, I truly believe that it is this mix of innovation and practice, of absorbing knowledge and sharing experiences, of science and fun, that makes our conference a fixed rendez-vous for so many radiation oncology professionals from Europe and around the globe.

When is the next meeting?
ESTRO 38 is scheduled next 26-30 April 2019 in Milan, Italy. It will be another occasion for all of us, radiation oncology professionals, to get together once again!

Looking forward to meeting you there!

Yolande Lievens
ESTRO 37 Chair

CLINICAL

INTRODUCTION

KARIN HAUSTERMANS

At this year's ESTRO annual congress many practice changing trials were presented, five of them in the late breaking abstract session. Three of these trials, the PORTEC-3, DAHANCA 10 and CRITICS, will be discussed in detail on the following pages.

The trials presented in the late abstract session reported on glioblastoma, breast cancer, lung cancer and prostate cancer.

The group from Dresden performed a prospective biomarker trial in 101 glioblastoma patients assessing the association of high methionine (MET) uptake post-operatively and outcome after radiotherapy and temozolomide. Patients without postoperative detection on the MET-PET, had a longer time to recurrence. Studies like this one can form the basis for focal dose escalation in this devastating tumour (Krause *et al*, Postoperative [11C]MET-PET predicts radiochemotherapy outcome in glioblastoma: a prospective trial)

The Danish Breast Cancer Group HYPO trial randomised 1883 patients with early breast cancer or DCIS between 50 Gy in 25 fractions and 40 Gy in 15 fractions. Multivariable analysis using grade 2-3 induration as an endpoint and including hypofractionation as a variable, identified large breast size as the only independent risk factor. Locoregional recurrences at 5 years were very low in both arms (Offersen *et al*, Hypo- vs normofractionated radiation of early breast cancer in the randomised DBCG HYPO trial).

UK investigators went one step further and tested one week of hypofractionated breast radiotherapy (27 Gy (whole breast) or 26 Gy (chest wall) in 5 fractions over one week), compared to 40 Gy in 15 fractions over 3 weeks in a phase III study (FAST-Forward). A tumour bed boost was given where indicated. Four thousand and ninety-six patients were randomised. Normal tissue effects were very low and comparable in both arms (Brunt *et al*, FAST-Forward phase 3 RCT of 1-week hypofractionated breast radiotherapy:3-year normal tissue effects).

A second abstract from the Danish Breast Cancer Group investigated the predictive value of tumour-infiltrating lymphocytes (TILs) in terms of benefit from radiotherapy in 1011 high risk breast cancer patients. High levels of pretreatment TILs interacted with radiotherapy to further improve overall survival but had no impact on local control. The authors suggest that this may be due to an abscopal effect induced by radiotherapy. Although the abscopal effect is fashionable these days we should be aware that these patients were treated between 1983 and 1989 so results should be extrapolated with care (Tramm *et al*, Tumour-infiltrating lymphocytes predicts improved overall survival after post-mastectomy radiotherapy)

Widmark and colleagues reported on the results of the Scandinavian non-inferiority Phase 3 HYPO-RT-PC trial on ultrahypofractionation. Twelve hundred patients with intermediate or high risk prostate cancer were randomised between conventional fractionation (39 fractions of 2 Gy over 8 weeks) and ultrahypofractionation (7 fractions of 6.1 Gy over 2.5 weeks). No androgen deprivation therapy was allowed. Ultrahypofractionation was found to be non-inferior. Both schedules resulted in a comparable low incidence of late side effects (Widmark *et al*, Ultrahypofractionation for prostate cancer: Outcome from the Scandinavian phase 3 HYPO-RT-PC trial)

First of all these trials prove that the radiation community still succeeds in randomizing large numbers of patients in Phase III trials studying a radiotherapy related question. The investigators should be congratulated for that!

Moreover, from the trials in breast and prostate cancer it is clear that we are moving steadily from conventional fractionated radiotherapy to hypofractionated radiotherapy. Classically trained radiation oncologists are reluctant to deliver doses per fraction larger than 2 Gy as they are concerned about late side effects. However, these trials together with many others published in the meantime clearly show that hypofractionated radiotherapy is not detrimental if patients are appropriately selected and certainly not when modern radiotherapy techniques are used such as IMRT and IGRT. Also the typical α/β values we assumed historically for tumours and late reacting tissues might in reality be different (lower for breast and prostate cancer, higher for late reacting breast tissue).

The radiobiology behind ultrahypofractionation is probably different from the radiobiology behind conventional fractionation. Ultrahypofractionation might induce an immune response and may even lead to a more pronounced abscopal effect. However, this requires more study as was alluded to in the symposia related to immune therapy and to the treatment of oligometastatic disease.

We should not underestimate the evolution in the way we deliver radiotherapy integrating image guidance and multifunctional imaging in the treatment process. This might also contribute to the success of hypofractionation.

The importance of IGRT although not in breast and/or prostate cancer was nicely illustrated in the study performed by the Christie NHS Foundation Trust, Manchester (see Johnson *et al* under awards for more detail).

Also the late breaking randomised Phase II PET-plan study in 205 non-small cell lung cancer patients reported that FDG PET-CT guided radiotherapy compared to conventional radiotherapy enabled higher dose escalation. This led to a clear trend in improved local control (Nestle *et al*, FDG-PET-guided target volume reduction for isotoxic dose escalation in LA NSCLC (PET-Plan study)

Emerging topics in the clinical track are the treatment of oligometastatic disease and the introduction of immune modulation in radiation oncology. Further research on MR guided and adaptive radiotherapy is ongoing. It is also clear that the radiation oncology community is preparing itself for the wide introduction of proton therapy. This will hopefully happen through international collaboration. Also the era of machine learning is rapidly evolving and finds its way into Oncology. The challenge for the future will be to validate these predictive models with external validation sets. Only through validated models we can individualize the treatment for the specific patient's cancer taking into account the patients' personal circumstances.

Congress report
For this congress report the four selected abstracts once more illustrate that randomised phase III trials remain the cornerstone of our knowledge and help us to improve the treatment and outcome of our patients.

The PORTEC-3 trial, De Boer *et al*, nicely illustrates the value of adding chemotherapy to radiotherapy in endometrial cancer in decreasing the risk of distant metastasis.

The analysis of patterns of recurrence in the CRITICS gastric cancer phase III trial, Verheij *et al*, showed that the cumulative incidence of recurrent disease at different sites is comparable between the two arms of the trial. The role of radiotherapy in the post-operative setting needs thus to be questioned.

Next to these two randomised trials a large study on residual setup errors after IGRT from the Christie NHS Foundation Trust, Manchester was submitted (Johnson *et al* reported under awards). It illustrates that residual setup errors are linked to overall survival in lung (n= 780) and esophageal cancer (independent validation cohort, n=177). Studies like this one form a strong case for patient advocacy groups to use to convince health providers to invest in the technology and in personnel to allow wide implementation of IGRT in our community.

Finally an ESTRO-HERO analysis, Defourny *et al*, on a TD-ABC model for estimating national cost and resource utilization in EBRT was selected. Studies like this one are of utmost importance to gain insight into the utilization of the available national resources and to predict the need for EBRT.

Karin Haustermans
Chair, SAG Clinical Radiotherapy

1. ENDOMETRIAL

Patterns of recurrence in the randomized PORTEC-3 trial of chemoradiotherapy for endometrial cancer

Stephanie M. de Boer[1*] MD, Melanie E. Powell[2] MD, Linda Mileshkin[3] MD, Prof Dionyssios Katsaros[4] MD, Prof Paul Bessette[5] MD, Christine Haie-Meder[6] MD, Petronella B. Ottevanger[7] MD, Prof Jonathan A. Ledermann[8] MD, Pearly Khaw[9] MD, Alessandro Colombo[10] MD, Prof Anthony Fyles[11] MD, Marie-Helene Baron[12] MD, Ina M. Jürgenliemk-Schulz[13] MD, Prof Henry C. Kitchener[14] MD, Prof Hans W. Nijman[15] MD, Godfrey Wilson[16] MD, Ilka Kolodziej[17] MPH, Silvestro Carinelli[18] MD, Ludy C.H.W. Lutgens[19] MD, Prof Vincent T. Smit[20] PhD, Naveena Singh[21] MD, Remi A. Nout1 MD, Karen W. Verhoeven-Adema[22] PhD, Prof Hein Putter[23] PhD, Prof Carien L. Creutzberg1 MD, on behalf of the PORTEC study group#.

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CONTEXT OF THE STUDY

The majority of women with endometrial cancer (EC) have a favourable prognosis. Approximately 15% of patients present with high-risk disease features and are at increased risk of distant metastases and EC related death. Standard adjuvant treatment for these high-risk patients has, for many decades been pelvic external beam radiotherapy. As previous trials showed no survival differences between chemotherapy and radiotherapy, and since higher pelvic recurrences were found after chemotherapy alone, combined adjuvant chemotherapy with pelvic radiotherapy was investigated. The chemoradiotherapy schedule that was found to be effective in a RTOG phase II study was used, in which pelvic radiotherapy is combined with 2 cycles of cisplatin (50 mg/m2 in weeks 1 and 4), followed by 4 cycles of carboplatin and paclitaxel.

OVERVIEW OF THE ABSTRACT

The randomised PORTEC-3 trial investigated the benefit of combined chemotherapy and radiotherapy (CTRT) compared to radiotherapy alone (RT) for women with high-risk EC, and balance benefit in overall survival and failure-free survival improvement and cost in terms of toxicity and impact on health-related quality of life (HRQL). Previous analysis of 2-year toxicity and HRQL showed significantly higher rates of adverse events and reduced HRQL during and after treatment in the CTRT arm, with rapid recovery but with persistence of grade 2 sensory neuropathy in 10%. (*de Boer et al; Lancet Oncology 2016*).

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

- The combination of chemotherapy and radiotherapy significantly improved 5-year failure-free survival by 7% (76% in the CTRT group vs 69% in the RT group). Women with stage III EC who had the highest risk of recurrence had the highest absolute failure-free survival benefit (69% vs 58% at 5 years). The differences in overall survival were not statistically significant.
- The majority of recurrences were distant metastases (22% CTRT vs 28% RT, of which 6% vs 10% occurred simultaneously with vaginal or pelvic recurrence), while isolated vaginal or pelvic recurrences were rare (0.3% and 1.2%).
- The median survival after any recurrence was 1.1 year after CTRT and 1.4 year after RT, while median survival after vaginal or pelvic recurrence was 1.2 vs 2.3 years (both not significantly different).

WHAT IMPACT COULD YOUR RESEARCH HAVE?

The failure-free survival improvement of 7% with combined adjuvant chemotherapy and radiotherapy supports

consideration of combined treatment for women with highest risk of recurrence, especially those with stage III EC. Nevertheless, the improvement in failure-free survival after CTRT should be weighed against the severity and duration of toxicity of combined treatment for each patient, especially since pelvic control was high and overall survival was not significantly improved. This CTRT schedule can thus not be recommended as a new standard for patients with stage I–II EC. Translational research will be done to determine the individual tumours' molecular profile in order to determine who benefits most from the combined treatment.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

For the interpretation of the final results of the PORTEC-3 trial, the results of the GOG-258 and the GOG-249 trials presented at ASCO and ASTRO 2017, are important. In the GOG-249 trial, women with stage I-II EC with high-intermediate or high-risk factors were randomly assigned to pelvic radiotherapy alone or to chemotherapy (three cycles of carboplatin/paclitaxel) followed by vaginal brachytherapy (Randall M. *et al*; ASTRO 2017). In the GOG-258 trial, patients with advanced EC were randomised to receive chemoradiotherapy or six cycles of carboplatin/paclitaxel (Matei D. *et al*; ASCO 2017).

Taken together, these three randomised trials show excellent pelvic control and relapse free survival rates with radiotherapy alone for women with stage I-II EC with high-risk features, and highest relapse-free survival and pelvic control rates with the combination of chemotherapy and radiotherapy for those with stage III disease.

2. GASTRIC

Patterns of recurrence in the CRITICS gastric cancer phase III trial

R.M. van Amelsfoort, K. Sikorska, E.P.M. Jansen, A. Cats, N.C.T. van Grieken, H. Boot, P.A. Lind, E. Meershoek-Klein Kranenbarg, M. Nordsmark, H.H. Hartgrink, H. Putter, A.K. Trip, J.W. van Sandick, H. van Tinteren, Y.H.M. Claassen, J.P.B.M. Braak, C.J.H. van de Velde, M. Verheij on behalf of the CRITICS Investigators

Netherlands Cancer Institute, Amsterdam, The Netherlands

CONTEXT OF THE STUDY

The mainstay of potentially curative treatment of gastric cancer is radical surgical resection. Because most patients in the Western world present with advanced stage disease, long-term survival remains poor with a five-year survival rate of around 25%. Postoperative chemoradiotherapy and perioperative chemotherapy have demonstrated a survival benefit over surgery alone. The multicenter randomised phase III CRITICS study (ChemoRadiotherapy after Induction chemoTherapy In Cancer of the Stomach) investigated whether postoperative chemoradiotherapy after neoadjuvant chemotherapy and adequate (at least D1+) surgery would improve overall survival (OS) in comparison with perioperative chemotherapy.

The study randomised 788 patients and no significant difference in overall survival was found (5- year OS 42% vs 40%). The CRITICS study investigated event-free survival, toxicity, health-related quality of life, and translational research as the secondary objectives.

Based on the results of the CRITICS study there are now two treatment options to consider for patients with resectable gastric cancer. Ongoing and future analyses should identify criteria for such selection.

OVERVIEW OF THE ABSTRACT

The aim of this abstract is to describe recurrence patterns in patients with resectable gastric adenocarcinoma treated with preoperative chemotherapy, surgery and postoperative chemotherapy or chemoradiotherapy within the multicenter randomised phase III CRITICS study. The analyses are performed according to intention-to-treat principle. Event-free survival was defined as time from randomization until disease progression before surgery, irresectable disease at surgery, tumour recurrence after potentially curative resection or death from any cause. Sites of progressive or recurrent disease were categorized as locoregional, peritoneal, distant or occurring at multiple sites (within a time span of 30 days).

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

- 474 events in 788 patients were observed at the time of analysis (median follow-up 5.1 years; 233 in the chemotherapy group and 241 in the chemoradiotherapy group). Most first events occurred within the first two years.
- Event-free survival rates at 2 and 5 years were 52% vs 51% and 39% vs 38% (chemotherapy vs chemoradiotherapy; stratified log-rank p = 0.92).
- Cumulative incidences of recurrent disease at different sites were comparable between postoperative chemotherapy and postoperative chemoradiotherapy (table 1). Within 2 years locoregional recurrence was detected in 16% of patients (7% locoregional only + 9% in combination with another site) in the chemotherapy group vs 16% of patients (5% locoregional only + 11% in combination with another site) in the chemoradiotherapy group.

WHAT IMPACT COULD YOUR RESEARCH HAVE?

Postoperative chemoradiotherapy did not improve overall survival or event-free survival for patients with resectable gastric adenocarcinoma treated with preoperative chemotherapy and adequate surgery compared to perioperative chemotherapy.

In the CRITICS study postoperative patient compliance was poor, as comparable with other studies, only approximately 50% of patients completed treatment as planned.

Because of the poor compliance in the postoperative phase of treatment, future studies should focus on optimizing preoperative treatment regimens. Therefore, the CRITICS II study, a multicenter randomised phase II trial, aims to identify the optimal preoperative regimen in operable gastric cancer by comparing three neoadjuvant treatment arms (chemotherapy vs chemotherapy and subsequent chemoradiotherapy vs chemoradiotherapy). All treatment arms will be followed by a resection with D2 lymphadenectomy.

We expect that by optimizing preoperative treatment, patient compliance will improve, significant tumour downstaging will be achieved and surgical radicality will increase.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

- The identification of subgroups based on specific patient and tumour characteristics will allow a more tailored treatment approach identifying those patients who will benefit most.
- Preoperative (chemo)radiotherapy is associated with acceptable toxicity, good patient compliance and improved outcome, and has become standard of care in an increasing number of indications.

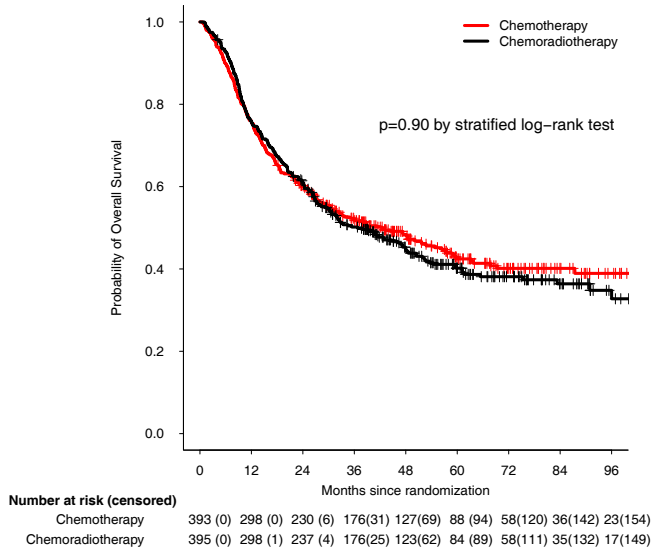

Figure 1. Overall survival

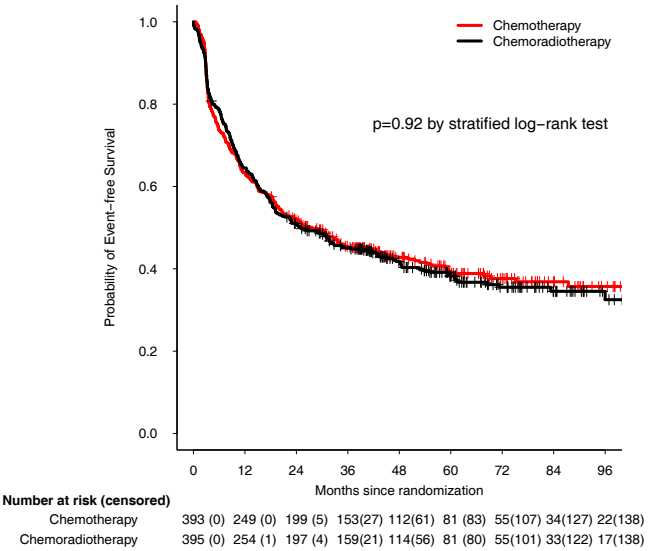

Figure 2. Event-free survival

	Events		CSC		CSCRT	
	CSC 233/393	CSCRT 241/395	CI (%) 2-year	CI (%) 5-year	CI (%) 2-year	CI (%) 5-year
Death (no recurrence)	40	36	7	10	5	9
Loco-regional (only)	35	27	7	9	5	7
Peritoneal (only)	50	61	12	13	15	16
Distant (only)	58	52	10	15	10	13
Multiple sites	50	65	11	13	15	17

Table 1. Number of events at each recurrence site together with cumulative incidences (CI) at 2 and 5 years from the competing risks analysis in patients who underwent preoperative chemotherapy, surgery and postoperative chemotherapy (CSC) or preoperative chemotherapy, surgery and postoperative chemoradiotherapy (CSCRT).

3. LUNG

Residual setup errors after IGRT are linked to overall survival in lung and oesophageal cancers

Corinne Johnson, Gareth Price, Corinne Faivre-Finn and Marcel van Herk

Manchester Academic Health Science Centre, The University of Manchester, The Christie NHS Foundation Trust

> *See under Awards on page 57*

4. HEALTH ECONOMICS

A TD-ABC model for estimating national cost and resource utilization in EBRT: an ESTRO HERO analysis.

N. Defourny[1], P. Dunscombe[2]†, J.M. Borras[3], M. Coffey[4], J. Corral[5], C. Gasparotto[6], L. Perrier[7], J. van Loon[8], C. Grau[9], Y. Lievens[1]

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CONTEXT OF THE STUDY / PRELIMINARY INFORMATION

In an era of constrained health care budgets, health economic evaluations are becoming increasingly important to support decision-making in the healthcare sector.
Along with the estimation of actual radiotherapy (RT) demand and forecast of future needs (described in Borras *et al.*, Radiotherapy & Oncology 2015 & 2016), cost accounting is a preliminary step in conducting any health economic evaluation such as cost-effectiveness, budget impact analysis or benchmarking within a reimbursement setting (Lievens *et al.*, Acta Oncol, 2015). However, reliable evidence about healthcare providers cost of radiotherapy is scarce (Defourny *et al.*, Radiotherapy & Oncology 2016).

OVERVIEW OF THE ABSTRACT

To tackle this knowledge gap, the HERO project estimates the cost of external beam radiotherapy (EBRT) service provision from the perspective of the healthcare providers with the purpose of informing decision-making. The cost of EBRT treatments and procedures is calculated with an online tool applying a time-driven activity-based costing (TD-ABC) methodology (Kaplan and Anderson, HBSP 2007). This conventional cost accounting methodology relies on the time required to perform RT procedures, hence the need for equipment and human resources. Acknowledging the broader context of EBRT, the tool also allows the user to identify the cost of other treatments (e.g. brachytherapy) or of activities supporting an optimal EBRT program (e.g. quality management).

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

While this paper highlights the potential of the model in a fictitious country Europalia, the practical application of this HERO cost accounting tool in the real-life setting provides National Radiotherapy Societies with the necessary data to empower radiotherapy at the national policy level.
Looking at the results of the study, the advantage compared to previously published literature is that it estimates the costs and resources needed at both national and treatment level:

- cost per EBRT treatment, on average and for various tumour types, treatment intents, fractionation schedules, techniques and complexities, which can be compared to the reimbursement system;
- total production cost of radiotherapy in a country, as a benchmark to the prevailing financing;
- number of resources required based on national patterns of care, including various techniques and fractionation schedules and on cancer population mix.

WHAT IMPACT COULD YOUR RESEARCH HAVE?

This costing model will enable the RT community, represented by the National Societies, to assess the cost of different EBRT treatment modalities and the required capacity and utilization of resources at the country level, in order to support reimbursement and resource planning decisions. Moreover, it will encourage the collection of up-to-date information about national RT care capacity (resources) and organization to serve a specific RT patient population.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

By providing radiotherapy professionals with evidence that can inform decision-making, this research is aligned with the recent increased interest in Cost-Effectiveness and Budget Impact Analyses. Indeed, it facilitates the cost assessment of specific clinical indications and can thus be used to complement clinical research with economical data. By focusing on the costing part of the value equation, defined as the best outcome for the money invested, it contributes to the creation of value to the patient, as advocated in the Value-Based Health Care Delivery framework developed by Prof. Michael Porter.

Figure 1. Structure of the model estimating the national cost of radiotherapy with TD ABC methodology.

PHYSICS

INTRODUCTION

MARCO SCHWARZ

The physics track for ESTRO 37 saw the continuation of a trend where new technological developments draw most of the attention of both participants who submit abstracts and reviewers who score them.
As a consequence, online MRI guidance, proton therapy, and also automatic planning, are going to have a prominent role in both the symposia and the sessions with proffered papers. Still, topics that are of traditional interest for physicists, such as basic dosimetry, radiobiological modeling and QA and audits, were well represented in a number of high quality abstracts.

Within the big picture quite focused on new technology, it is worth mentioning that the highest scoring physics abstract, which was also the winner of the Donald Hollywood award, somehow departs from the general trend, showing how physicists don't need the latest and greatest technological gadgets to produce remarkable and very relevant work. Johnson and colleagues, in fact, managed to demonstrate how image guidance tools available to most of us can have a positive impact on an endpoint as crucial as survival, at least for the category of patients included in their study.

In the following pages you will find five selected abstracts which were presented in oral sessions, to give you an overall impression of the breadth and depth of topics covered in our physics track.

Bijman and colleagues performed a study on NTCP-model based patient selection for hypo-fractionated prostate treatment. The so-called model based approach to patient selection was proposed in the context of proton therapy but it can be applied to the whole of radiation oncology. This study also relied on automatic planning, thus showing the benefits of combining systematic criteria for patient selection with consistent planning quality on a large scale.

Moennich *et al* explored the potential of high-field MR-linac for hypoxia dose escalation in head and neck cancer, via an in-silico study. The authors tested the dose shaping capabilities of this new device in very complex situations, finding that the MR-linac plans are slightly less conformal and inferior in OAR sparing to VMAT plans on a conventional linac. These differences are however small, and the authors think that these small disadvantages may in the future be compensated by margin reduction due to MR-based daily adapted radiotherapy and implementation of VMAT on the MRI Linac.

The work by von Münchow *et al* addresses the issue of interplay between respiratory motion of a tumour and dose delivered by complex radiotherapy. They developed a method that combines Monte Carlo dose calculation and dose accumulation on 4D datasets and that allows the simulation of arbitrary respiratory curves sampled at 0.2s intervals, with the aim of providing information on the possible dosimetric effects for a broad spectrum of breathing motions.

The relation between dose and cardiac substructures and clinical outcomes in non-small cell lung cancer chemoradiotherapy is a 'hot topic' in dose modeling, and it is addressed in the study by Thor and colleagues. The group from Memorial Sloan Kettering analyzed the dose to 13 cardiac substructures for 179 patients, combining dosimetric and clinical variables in their analysis. Their results suggest that limiting the low dose-bath to the cardiovascular system is important to prolong survival after chemo-radiation for NSCLC.

Kostiukhina *et al* worked on the characterisation of a phantom for 4D applications in ion beam therapy. Treating moving targets with heavy charged particles is even more difficult than with photons, and the need for reliable experimental data is crucial for the validation of both dose calculation and the overall treatment workflow. The results from the group from Vienna/Wiener Neustadt show a fair agreement between Monte Carlo dose calculation and measurements with different detectors.

Marco Schwarz
Chair, SAG Radiation Physics

1.

NTCP-model based patient selection for hypofractionated prostate treatment – A computer simulation

Rik Bijman[1], Abdul Sharfo[1], Wilco Schillemans[1], Wilma Heemsbergen[1], Marnix Witte[2], Floris Pos[2], Luca Incrocci[1], Ben Heijmen[1]

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CONTEXT OF THE STUDY

Between 2007 and 2010 the HYPRO study, a multicenter randomised phase 3 hypofractionation trial for intermediate- and high-risk prostate cancer treatment has been executed in the Netherlands. Patients were randomised between hypofractionation (19 fractions of 3.4 Gy) and conventional fractionation (39 fractions of 2 Gy). Non-inferiority of hypofractionation for late genitourinary (GU) and gastrointestinal (GI) toxicity was hypothesized but could not be proven[1]. All study patients were manually planned. In a previous study[2], we demonstrated the clinical advantages of automated treatment planning for this group of patients.

OVERVIEW OF THE ABSTRACT

In this study, we automatically generated plans for both hypofractionated and conventional treatment, for each of the 725 involved patients. Normal tissue complication probabilities (NTCP) were then calculated for the two treatments, using NTCP models that were derived from late toxicity scored in the HYPRO study. The calculated NTCPs were used to investigate strategies for selection of patients for hypofractionation (with increased NTCP). We performed computer simulations to establish percentages of patients that would be treated with hypofractionation, as a function of acceptance threshold for increases in calculated NTCP relative to conventional fractionation.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

The percentage of patients treated with hypofractionation strongly depended on the acceptance thresholds for GU and GI toxicity. For GU and GI NTCP thresholds of 4.6% and 2.4% respectively, 50% of patients would be treated with hypofractionation.

WHAT IMPACT COULD YOUR RESEARCH HAVE?

The enormous reduction in workload of automated compared to manual treatment planning is an important benefit. This gives the opportunity to generate multiple treatment plans per patient for different fractionation schemes or treatment modalities from which the optimal can be chosen based on NTCP. This work helps in visualizing the accepted increase in complication probability while aiming for a specific percentage of patients to be selected for a new treatment. So, with a low workload a generic and uniform way of assigning patients to their optimal treatment seems possible.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

Personalized medicine is currently an import topic in radiotherapy. Choosing the optimal treatment for every single patient would be ultimate. On the other hand, due to capacity and money limitations it might be necessary to select for certain expensive treatments (e.g. proton therapy) only those patients that benefit most. Unbiased automated planning, as proposed in this study, can help in the decision making.

REFERENCES

[1] Aluwini S, Pos F, Schimmel E *et al.* Hypofractionated versus conventionally fractionated radiotherapy for patients with prostate cancer (HYPRO): acute toxicity results from a randomized non-inferiority phase 3 trial. *Lancet Oncol 2015*;16:274-83.

[2] Sharfo AW, Dirkx M, Bijman R *et al.* Late toxicity in HYPRO randomized trial analysed by automated planning and intrinsic NTCP-modelling. (Abstract), ESTRO 36; OC-0251

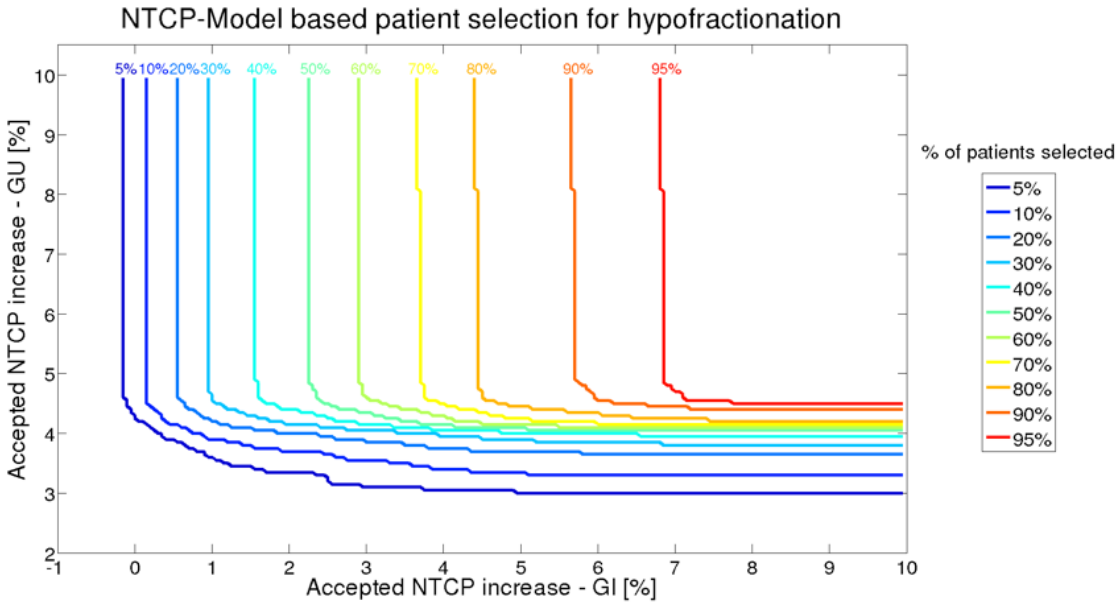

Figure 1. Percentages of patients selected for hypofractionation as a function of accepted GU and GI NTCP increases. Depicted curves represent iso-percentage lines.

2.

High-field MR-linac treatment plans for hypoxia dose escalation in head and neck cancer

David Mönnich, Marcel Nachbar, Eric Neuhaus, Cihan Gani, Simon Boeke, Stefan Welz, Daniel Zips, Daniela Thorwarth

Department of Radiation Oncology, University Hospital and Medical Faculty, Eberhard Karls University Tübingen, Germany

CONTEXT OF THE STUDY

Hybrid devices combining a high-field MRI scanner and a linear accelerator (MRI-linac) for radiotherapy (RT) are becoming mature for clinical use. The high quality anatomical MR images are intended to increase the geometrical accuracy of RT, but MRI-linac technology can also be used for integrating online functional MRI into the RT workflow. This might be useful to steer a local RT dose escalation (DE) aimed at hypoxic, i.e. radioresistant, tumour regions. Hypoxia DE is evaluated in trials based on offline hypoxia PET imaging. MRI-linac technology might complement or replace hypoxia PET information and increase the accuracy of the application of DE.

OVERVIEW OF THE ABSTRACT

MRI-linac devices, e.g. the 1.5 T MRI-linac by Elekta AB, Stockholm, Sweden, differ from standard linacs in some technical aspects, which can influence the quality of the applicable dose distributions with respect to target coverage and organ at risk doses. In this retrospective study we compared the treatment plan quality between the MRI-linac and a standard linac for RT of ten consecutive head and neck cancer patients who were treated in a hypoxia DE trial at our institution. This is important, because initial MRI-linac trials using standard treatment protocols will likely assume that a similar plan quality is achieved.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

It was possible to create clinically acceptable plans for both devices for all patients (Figure 1). For one patient the longitudinal extension of the target volume exceeded the limits of the MRI-linac. Plans were optimized for similar target coverage, resulting in slightly increased organ at risk doses for MRI-linac plans, e.g. in parotid glands and skin. Generally, MRI-linac plans were less conformal, which in the future might be improved by technological advances, e.g. by VMAT instead of step-and-shoot technique. Comparable mean DE doses were achieved in hypoxic subvolumes.

WHAT IMPACT COULD YOUR RESEARCH HAVE?

The results of this planning study show that treatment of head and neck cancer patients including a DE to hypoxic subvolumes appears feasible with current MRI-linac technology for most patients with a treatment plan quality close to that of a modern standard linac. In a further step, the anticipated advantages of the MRI-linac have to be evaluated. Geometrical precision might allow for reduced margins, potentially resulting in less toxicity and higher precision in the application of RT including DE. Functional MRI integrated in the RT workflow potentially allows for further individualization and could reduce the patient burden from offline imaging, e.g. hypoxia PET. In research, imaging trials including frequent MR imaging will be facilitated.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

Personalized therapy is a major trend in oncology. The amount of available individual data from imaging, biomarkers or genomics is increasing, but application of this knowledge to individualize therapy is lagging behind for various reasons. For example, integrating advanced imaging data into RT treatment planning requires a very precise treatment application that might require new technology such as the MRI-linac. Furthermore, imaging trials are becoming more complex and imaging is performed more frequently before and during therapy. Consequently, it can be a big advantage to perform online MR imaging during RT. In summary, the MRI-linac is a great research tool for imaging-based treatment individualization and promises prompt increases in geometrical accuracy by integrating high quality online imaging.

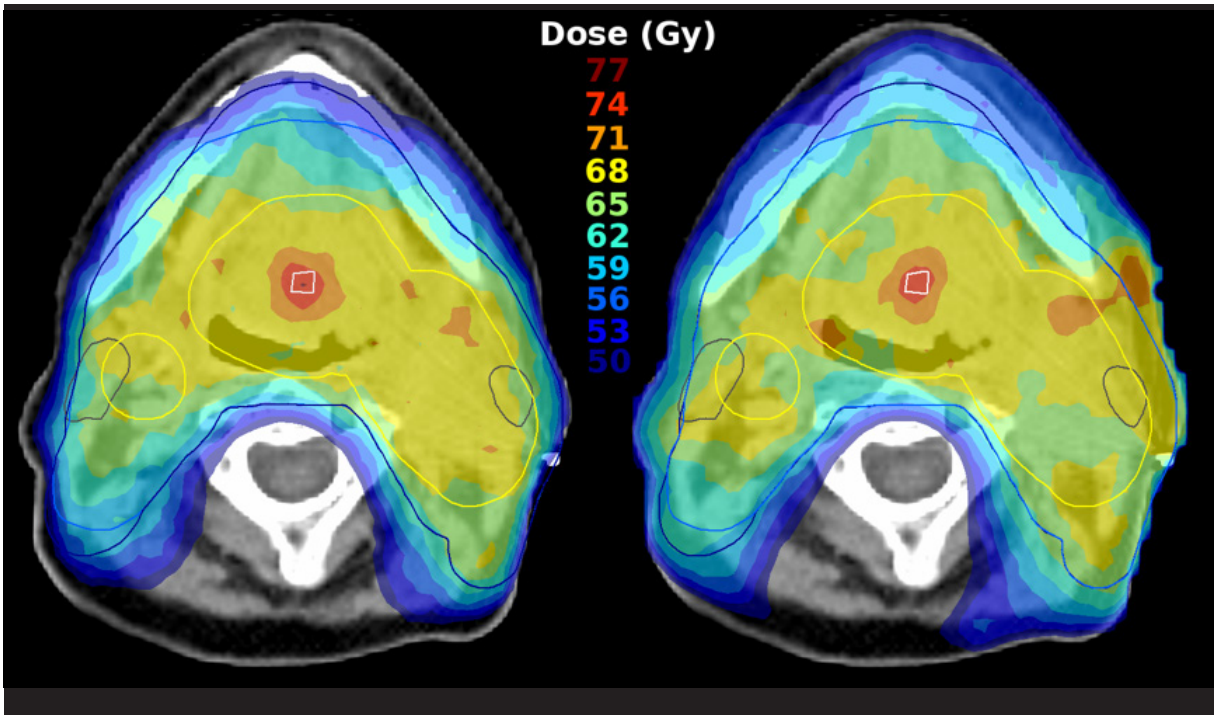

Figure 1. Exemplary dose distributions including local DE for a standard linac (left) and the MRI-linac (right). Contours of escalated volume, PTV_{70}, PTV_{60}, PTV_{54} and parotid glands are shown.

3.

Random breathing states sampling in a 4D MC dose calculation framework to quantify interplay effects

Asmus von Münchow[1], Katrin Straub[1], Christoph Losert[1], Roel Shpani[1], Jan Hofmaier[1,2], Philipp Freislederer[1], Christian Heinz[1], Christian Thieke[1], Matthias Söhn[1], Markus Alber[3,5], Ralf Floca[4,5], Claus Belka[1,6], Katia Parodi[2], Michael Reiner[1], Florian Kamp[1]

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CONTEXT OF THE STUDY

Breathing-induced, intrafractional tumour motion is an ongoing challenge for precise radiotherapeutic treatment of lung tumours. Typically, Stereotactic Body Radiotherapy (SBRT) is applied to precisely deliver the prescribed dose to the tumour. Due to tumour motion the target volumes are adjusted to cover the whole range of motion of the moving target (so called Internal Target Volume (ITV) approach).

3D-Conformal radiotherapy (3D-CRT) is the most robust irradiation technique for lung SBRT. Advanced techniques like Volumetric Arc Therapy (VMAT) allow for better dose conformality. In contrast to 3D-CRT, radiation is delivered during gantry rotation with dynamically changing shape and fluence of applied fields. The beam intensity is modulated by successive application of small fields.

The interplay between respiratory motion of the tumour and delivery of small fields in VMAT may lead to unintended and unintuitive dose deviations from the intended plan. Fig. 1 illustrates this phenomenon leading to so called interplay effects. To safely apply VMAT for lung SBRT, it is thus desirable to quantify dose deviations and uncertainties introduced by interplay effects.

OVERVIEW OF THE ABSTRACT

We present a 4D-dose recalculation tool to precisely simulate the dose distribution for a moving target volume. It combines Monte Carlo (MC) dose calculation, Elekta Delivery Parameter Log Files and dose accumulation based on 4D-CT images: Treatment plans are sampled in small time fragments and calculated on ten 4D-CT phases. Arbitrary respiratory movements are simulated with the obtained dose fragments by 4D-CT phase allocation and dose accumulation based on deformable image registration in AVID, a novel software system for automated processing and analysis of radiotherapy data. Statistical evaluation of various treatment start phases (i.e. phase shifts of the patient's breathing curve) and random assignments of breathing states are applied to quantify interplay effects.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

- A comprehensive tool has been developed for interplay-sensitive 4DCT Monte Carlo dose recalculation and simulation of arbitrary respiratory motion for patient cases.
- Interplay induced statistical blur in dose coverage can be determined by simulating a wide range of breathing scenarios with random breathing states assignment, selected for every 0.2 s dose fragment. In contrast to VMAT, the 3D-CRT technique is not prone to interplay effects (cf. fig. 2-3).
- It is not necessary to include the actual breathing curve of the patient (with random start phase shifts) in the interplay evaluation. Comparing fig. 3 and fig. 4 it can be concluded that a random state assignment sufficiently covers possible interplay effects.

WHAT IMPACT COULD YOUR RESEARCH HAVE?

The presented tool provides a framework for highly accurate dose recalculation and simulation for moving lung tumours. A time resolved VMAT delivery for an exemplary patient case is shown in the video linked in fig 5. The right panels display the accumulated dose obtained with the presented tool. Interplay between tumour motion and dynamic dose application can now be comprehensively quantified based on MC calculations and used for treatment plan analysis and evaluation. The presented methods will help to gain confidence in using modern treatment techniques like VMAT for lung SBRT.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

With the introduction of dynamic treatment delivery techniques for moving tumours it is necessary to identify and quantify interplay effects, eventually with precise MC dose calculations. VMAT offers the great advantage to combine high dose conformality with fast treatment deliveries. Hence, delivery of VMAT SBRT plans is a current trend in radiation oncology. With the presented work we introduce the possibility to comprehensively simulate and quantify the effect of inherent interplay effects based on accurate MC dose calculations.

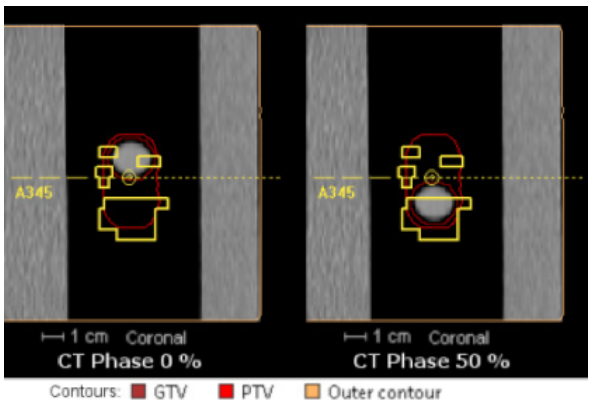

Figure 1. Illustration of the possible interplay effect for delivery of small VMAT fields to a moving tumour of a CIRS Dynamic Thorax Phantom. Depending on the breathing phase, the field (yellow boundaries) may "miss" the tumour (left) or "cover" it (right).

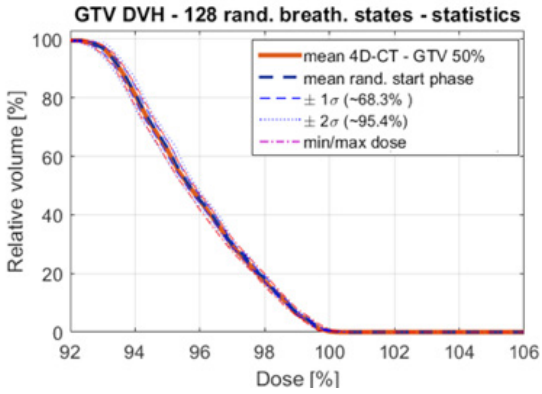

Figure 2. Dose volume histograms (DVHs) showing the time-resolved, accumulated dose of 3D-CRT SBRT to the reference GTV (end-of-expiration phase): original plan (ITVMIP), mean 4D-CT dose and 128 random breathing states simulations. As expected, almost no interplay effects are visible in 3D-CRT, due to the large fields in this technique.

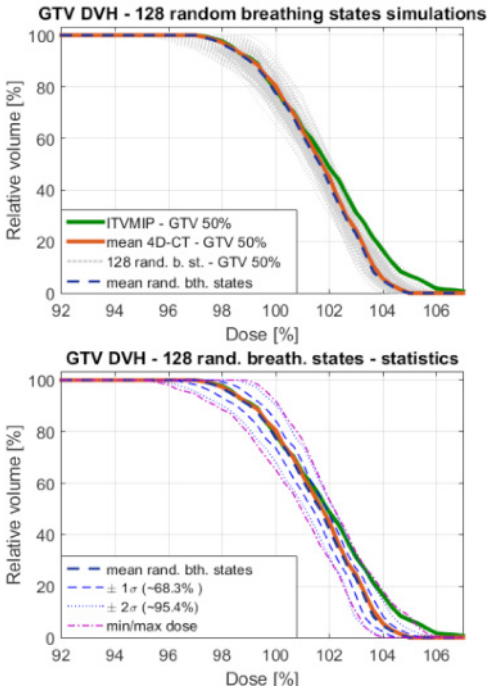

Figure 3. DVHs showing the dose of VMAT SBRT to the reference GTV (end-of-expiration phase): original plan (ITVMIP), mean 4D-CT dose and 128 random breathing states simulations.

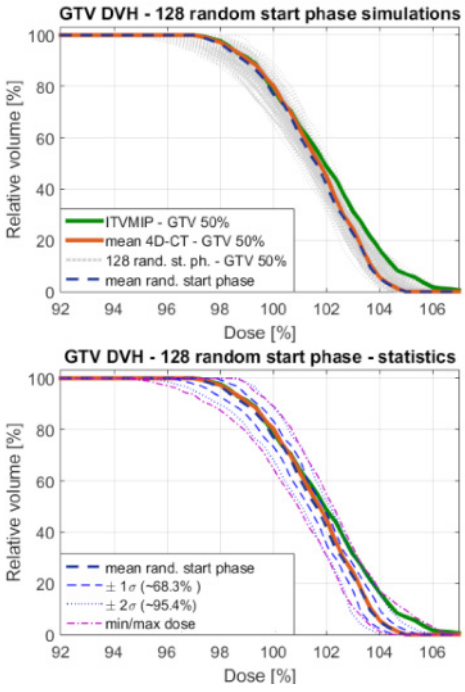

Figure 4. Same as fig. 3 but for 128 random treatment start simulations.

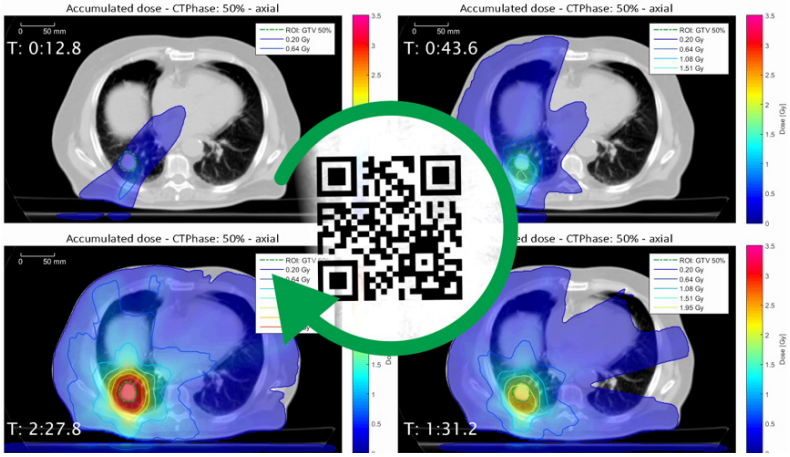

Figure 5. VMAT delivery for an exemplary patient case on YouTube: https://youtu.be/X6xV5qV988g (➔ scan QR-code) Elekta Delivery Log Files are turned into dose fragments (displayed in the left panels of the video). Dose fragments are accumulated with AVID according to breathing curve (displayed in the right-hand panels).

4.

Dose to cardiac substructures predicts survival in non-small cell lung cancer chemo-radiotherapy

Maria Thor, Alexandra Hotca, Andrew Jackson, Ellen Yorke, Andreas Rimner, and Joseph O Deasy

Memorial Sloan Kettering Cancer Center, USA

CONTEXT OF THE STUDY

Recently, a handful of studies have been published in support of radiation dose to the heart shortening survival after chemo-radiotherapy (CRT) for non-small cell lung cancer (NSCLC). This study aimed to test this hypothesis for overall survival (OS), and further shed light on the involvement of dose to specific cardiac substructures. A subsequent aim was to investigate this approach for non-cancer specific survival (NCS). The data was accumulated at one institution over a ten-year period, and a total of 241 patients were included. A thorough modelling approach including Bootstrapping was carried out, and one best dose metric/substructure was considered.

OVERVIEW OF THE ABSTRACT

Dose to cardiac substructures rather than dose to the whole heart predicted both survival endpoints. More specifically, candidate risk factors for both endpoints were low dose to the aorta, and the left atrium, high dose to the left ventricle, as well as unfavourable performance status. Additional candidate risk factors for OS were low pulmonary artery dose, high dose to the lung and smoking currently. For NCS, the low lung dose bath, as well as pre-existing cardiovascular disease were additional candidate risk factors.

The two models finally selected for OS included aortic dose sparing together with either unfavourable performance status or smoking currently. The corresponding two final models for NCS were 'dose only' models, and also included aortic dose sparing but instead together with low left atrial dose, or high left ventricular dose.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

Dose to cardiac substructures rather than dose to the whole heart predicted both survival endpoints. More specifically, candidate risk factors for both endpoints were low dose to the aorta, and the left atrium, high dose to the left ventricle, as well as unfavourable performance status. Additional candidate risk factors for OS were low pulmonary artery dose, high dose to the lung and smoking currently. For NCS, the low lung dose bath, as well as pre-existing cardiovascular disease were additional candidate risk factors.

The two models finally selected for OS included aortic dose sparing together with either unfavourable performance status or smoking currently. The corresponding two final models for NCS were 'dose only' models, and also included aortic dose sparing but instead together with low left atrial dose, or high left ventricular dose.

WHAT IMPACT COULD YOUR RESEARCH HAVE?

Our findings suggest that limiting dose to the cardiovascular system, and in particular sparing the aorta, the left atrium, and the left ventricle have implications in prolonging survival after chemo-RT for NSCLC. Performance status and smoking status assessments, together with cardiovascular functional tests prior to treatment could further guide in treatment protocol stratification.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

Limiting dose to specific cardiac substructures in the time frame of being clinically feasible would require fast and accurate segmentation algorithms. Deep learning-based segmentation algorithms are likely to have a central role in achieving this. Another key component to further reduce dose to the cardiovascular system is the use of state-of-the-art planning and delivery techniques together with careful image-guidance.

5.

Characterization of a novel breathing phantom for 4D applications in ion beam therapy

N. Kostiukhina[1], M. Clausen[1], M. Stock[2], D. Georg[1], B. Knäusl[1]

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CONTEXT OF THE STUDY

The in-house developed anthropomorphic respiration phantom ARDOS (Advanced Radiation DOSimetry) was developed for the investigation, improvement and verification of 4D applications in radiation oncology including different treatment techniques, as well as various imaging aspects. The phantom is made from tissue equivalent materials and suitable to insert active and passive detectors to the lung tumour volume. Lung expansion as well as independent motion of the tumour replica and ribs can be simulated. The ARDOS phantom was recently tested and benchmarked for 4D photon therapy and several imaging techniques (Kostiukhina et. al. 2017 PMB 62:8136-8153). The aim of the current work was the extension towards 4D proton therapy with focus on dose validation using different detector types.

OVERVIEW OF THE ABSTRACT

In order to test the usability of the phantom for 4D dose validation in proton radiotherapy, the following aspects were investigated:

- CT image parameters of the tissue equivalent phantom materials and their stopping power characteristics when assigning their physical properties (mass density, mean ionization energies and atomic mass composition) directly by overwriting the materials in the CT scan or by applying the clinical CT calibration curve,
- Characterisation of a static dosimetry system - ARDOS with detectors (pin point ionization chamber (PP), thermoluminescent dosimeters (TLD)), in a proton Spread Out Bragg Peak (SOBP) (Figure 1),
- Determination of the dose calculation accuracy of a state-of-the-art treatment planning system in simulated lung set-ups, with a focus on Monte Carlo (MC) and Pencil Beam algorithms.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

- High dose deviations (up to 40% of prescribed dose outside the target volume) were observed when assigning physical properties out of a look up table in comparison with the clinically used density-stopping power calibration curve (Figure 2).
- The MC calculated dose agreed with the PP chamber measurements within 3% in the static situation (tolerance level of beam model validation measurements). The detector, therefore, was determined as suitable for future 4D dosimetry in scanned proton beams. Dose parameters from TLDs deviated from the MC calculated dose by a higher amount due to the higher resolution and the sensitivity towards tissue interfaces.
- The Monte Carlo dose calculation algorithm (optimization and final dose calculation) was superior to the Pencil Beam when benchmarked against PP measurements.

WHAT IMPACT COULD YOUR RESEARCH HAVE?

Phantom-based dose assessment is necessary for both the verification and clinical implementation of upcoming 4D techniques in radiation oncology with actively scanned particle beams, including comprehensive end-to-end test procedures. However, due to the lack of available phantoms fulfilling all requirements for ion beam therapy, there is the need for characterizing phantoms' dosimetric properties for dose calculation and validation measurements. Our experience can be an example of how such a sophisticated dosimetric tool can be utilized for emerging radiotherapy techniques with focus on 4D in-silico and experimental investigations. Completing the presented investigations with penumbra and SOBP measurements in the moving system will contribute to the first step towards clinical implementation of 4D treatments at the MedAustron Center for Ion Beam Research and Therapy.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

Scanned particle beam therapy has the potential to improve clinical outcome for lung, liver and pancreas cancer. As these entities are affected by respiratory motion, 4D dose calculation and its dosimetric validation are essential research and development topics in particle therapy; moreover the clinical implementation of particle therapy for moving targets is envisaged by many centers. With the improvement of 4D imaging techniques as well as particle beam dose calculation, tools for dosimetric validation have to fulfill high requirements towards realistic motion representation and material composition. The presented study is a pioneer for future phantom development with respect to 4D QA measurements and end-to-end test procedures. Looking towards the trend of MR guided particle therapy detailed phantom and material investigations are the basis for the development of MR compatible phantoms.

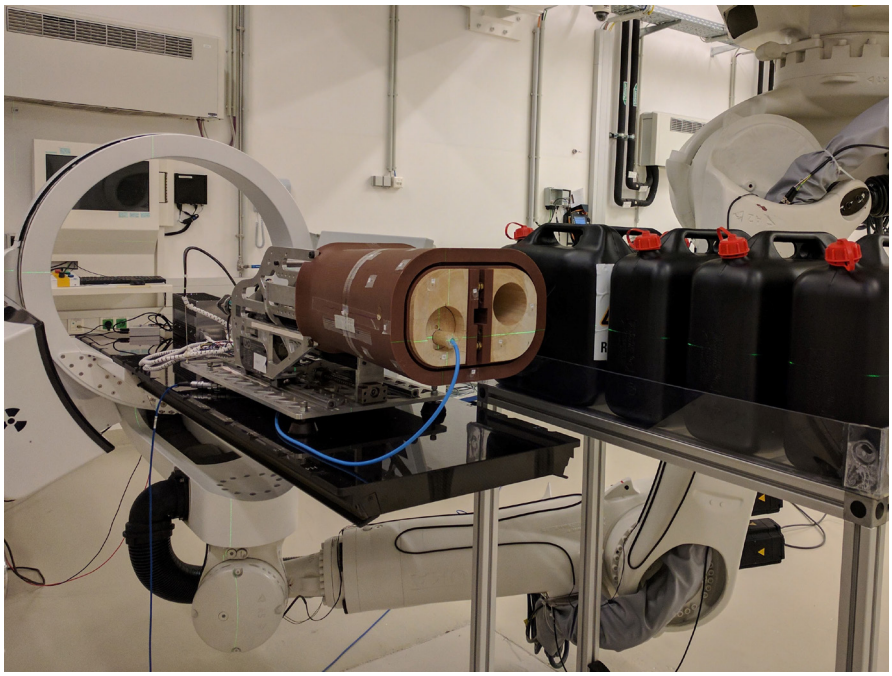

Figure 1. Experimental setup: ARDOS with inserted pin point ionization chamber

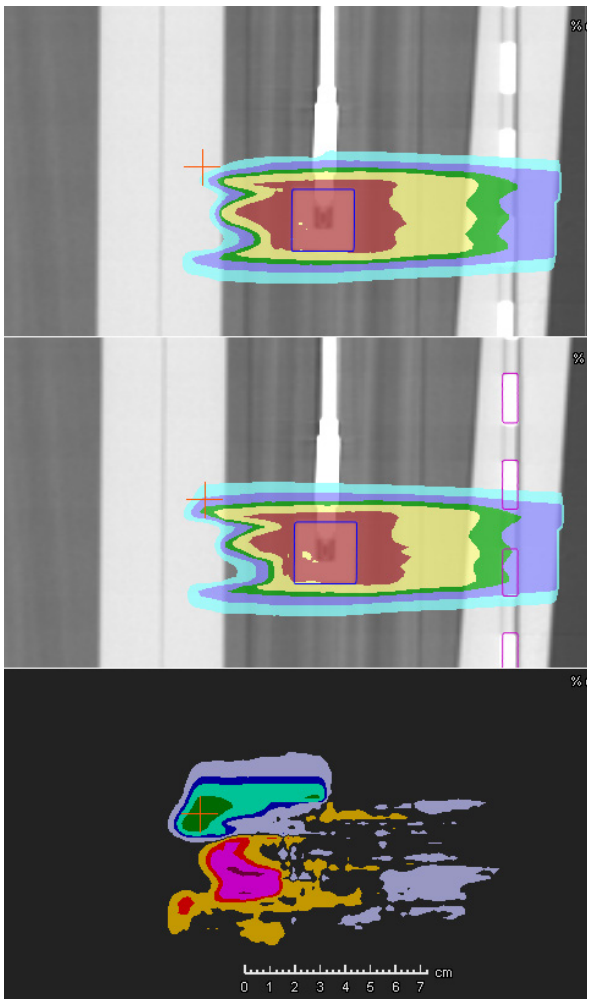

Figure 2. Dose distribution for phantom's geometry with tissue characterized by assigning physical properties out of a look up table (middle) and from the clinical electron density-stopping power conversion curve (top). Relative dose difference between the two treatment plans.

2ND ESTRO PHYSICS WORKSHOP

Science in development

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Early registration:
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BRACHYTHERAPY

INTRODUCTION

CHRISTIAN KIRISITS

This year's brachytherapy track included lectures on teaching the state of the art, reporting of clinical evidence and innovative new developments.

The first teaching lecture focused on the use of imaging to achieve better brachytherapy results. Although most brachytherapy techniques nowadays are performed with image guided treatment planning, there is potential for improvement by combining different image modalities for pre-planning the implantation, guiding the applicator placement, dose planning and dose delivery verification. The second teaching lecture focused on oesophageal cancer, a disease site where the evidence for brachytherapy is well documented. These types of lectures create awareness of the high potential of brachytherapy and showcase the state of the art use of less common brachytherapy treatments.

In contrast, adjuvant vaginal brachytherapy in endometrial cancer is a very common brachytherapy procedure which is performed in high patient numbers. However, there is heterogeneity in treatment approaches across Europe. A dedicated symposium discussed the need for brachytherapy in this situation including pro and cons, and experience with different risk groups and decision making. After this symposium, an entire proffered papers session was dedicated to the large number of high quality abstracts on gynaecological brachytherapy. As in previous years, several abstracts came from the EMBRACE studies, a success story illustrating the good collaboration initiated under the umbrella of the GEC-ESTRO GYNAE working group.

On Saturday afternoon, the quality assurance in brachytherapy session included updates on error management and recommendations, and how new equipment like innovative in-vivo dosimetry can further support this important process. The symposium was followed by a proffered paper session focusing on new technology including online source localisation, applicator tracking, scintillation detectors, dynamic modulation with shielded applicators, dose accumulation and radiomics.

The Sunday morning session had presentations from experts on cosmetic appearance after brachytherapy. After an introduction on how to measure cosmetic outcome, the session focused on specific disease sites with breast, pediatric head & neck and skin brachytherapy.

The proffered paper session that followed included the top abstracts for prostate and head and neck. Prostate topics include external beam and HDR combinations, single fraction monotherapy and salvage treatment. This again demonstrates the large variety of possible options with brachytherapy. The head and neck topics included cancer of the nasal vestibule and uveal/choroidal melanomas. The highlight was the ESTRO-Elekta Brachytherapy award for Tagliaferri *et al* (see the report under awards) for their predictive model for visual loss after uveal melanoma brachytherapy.

For prostate, a dedicated symposium discussed LDR versus HDR brachytherapy including dosimetry and equieffective dose, long term results for each type of treatment and a direct comparison in a prospective phase III study.

The last proffered paper session in the brachytherapy track covered mainly breast treatments. Boost and accelerated partial breast experience with high patient numbers and detailed research hypotheses will be presented. The GEC-ESTRO Best Junior presentation sponsored by Elekta Brachytherapy was awarded to Cavallin *et al.* (see the report under awards) for a well performed paper on the transition from 2D to 3D planning. Special mention is made of one highly-scored paper from a group from Pakistan on HDR intraluminal brachytherapy for rectal cancer.

The poster discussion session for brachytherapy was on pelvic brachytherapy including anal, prostate and cervical cancer. The selection of papers is based on the peer-review scores for the submitted abstracts.

Again I would like to emphasise that we are continually looking for high quality abstracts for our proffered paper sessions and we would encourage the many individual initiatives to share their experience. The GEC-ESTRO working groups and workshops are also opportunities to network and work on joint initiatives.

I would like to thank all the authors, reviewers and members of the Scientific Advisory Group for their immense work in creating the brachytherapy track of ESTRO 37.

Christian Kirisits
Chair, SAG Brachytherapy

1.

A predictive model for visual loss after uveal melanoma interventional radiotherapy (brachytherapy)

L. Tagliaferri[1], M.M. Pagliara[2], J. Lenkowicz[1], R. Autorino[1], A. Scupola[2], M.A. Gambacorta[1], L. Azario[3], D. Giattini[2], V. Lancellotta[4], M. Ferioli[5], V. Valentini[1], M.A. Blasi[2].

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[4]University of Perugia and Perugia General Hospital, Radiation Oncology Section- Department of Surgical and Biomedical Science, Perugia, Italy.
[5]University of Bologna, Radiation Oncology Center- Department of Experimental- Diagnostic and Specialty Medicine - DIMES, Bologna, Italy.

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> See under Awards on page 63

2.

External beam (EBRT) and HDR brachytherapy (BT) in prostate cancer: impact of EBRT volume

H Tharmalingam, Y Tsang, A Choudhury, PJ Hoskin on behalf of the National UK HDR brachytherapy database

Mount Vernon Cancer Centre, Northwood, UK; The Christie Hospital NHS Trust, Manchester, UK

CONTEXT OF THE STUDY

For patients with high-risk prostate cancer, the risk of occult lymph node metastases in the pelvic lymph nodes can be as high as 40%. Whole pelvis radiotherapy (WPRT) as opposed to prostate-only radiotherapy (PORT) may improve outcomes in the high-risk population by sterilization of micrometastatic pelvic nodal disease. However, the use of WPRT remains controversial with two prospective randomised trials comparing WPRT and PORT proving negative[1,2]. A unifying limitation of both of these studies was the cumulative prostatic doses of 66-70Gy which would now be deemed sub-optimal in the modern dose-escalation era. With inadequate local control, any potential benefit of regional nodal irradiation may be lost.

OVERVIEW OF THE ABSTRACT

Interstitial brachytherapy has been successfully employed as a means of intensifying local dose to the prostate. The sharp fall-off in dose combined with dose heterogeneity across the brachytherapy volume can result in dose escalation to some areas of the gland to greater than 140Gy EQD2. Through escalation of intra-prostatic dose with HDR brachytherapy, the true value of concurrent pelvic treatment may become apparent.

A national database evaluating prospectively a standard protocol in the multicentre setting has been collecting data in the UK. Within this two external beam schedules are permitted: 46Gy in 23 fractions WPRT or 37.5Gy in 15 fractions PORT. A single dose HDR boost of 15Gy is given in all cases. We have analysed this database to explore the impact of EBRT volume (WPRT vs PORT) on biochemical progression-free survival (bPFS) and urinary and bowel adverse effects when given in combination with HDR brachytherapy to treat intermediate and high-risk prostate cancer patients.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

812 patients were recruited. 411 received EBRT to the prostate only; 401 received WPRT to the level of the common iliac chain. Median follow-up was 4.5 years; 5-year bPFS rates for the WPRT versus the PORT arms were 89% vs 81% ($p = 0.007$) for all patients and 84% vs 77% ($p = 0.001$) for high-risk patients (Figure 1). Differences in bPFS remained significant ($p = 0.001$) after accounting for Gleason score, presenting PSA, T stage and ADT duration as co-variates. There was no difference in overall survival. Compared to PORT, WPRT resulted in increased acute urinary toxicity ($p = 0.03$) but not acute gastrointestinal toxicity ($p = 0.06$). No difference in late radiation toxicity was observed.

WHAT IMPACT COULD YOUR RESEARCH HAVE?

This is the largest study to date evaluating WPRT in high-risk patients treated with aggressive local dose escalation by delivery of a HDR brachytherapy boost. The positive findings make it timely to re-open the debate regarding WPRT in high-risk disease. Advanced radiotherapy techniques such as intensity modulated radiotherapy will now allow for dose escalation to the pelvic nodes without increased toxicity, potentially improving clinical outcomes. Moreover, modern mapping studies using magnetic resonance (MR) lymphography and single photon emission computed tomography (SPECT) have shown a significant proportion of patients to have positive lymph nodes outside of standard target volumes. With MR-guided radiotherapy and vastly improved image registration, we could also see high-dose delivery to these nodal groups, further improving outcomes. In the context of dose escalation with brachytherapy, novel imaging modalities and advanced radiotherapy, WPRT may therefore play an increasingly important role in the management of high-risk prostate cancer.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

A brachytherapy boost is seen as the best means of dose escalation in the prostate supported by two randomised trials, one using HDR[3] and the other low-dose rate (LDR)[4]. The place of WPRT in radiotherapy for intermediate and high-risk patients is now the subject of two prospective randomised controlled trials, PIVOTAL BOOST in the UK and RTOG 0924, the results of which will inform future strategies for the external beam volume in this population.

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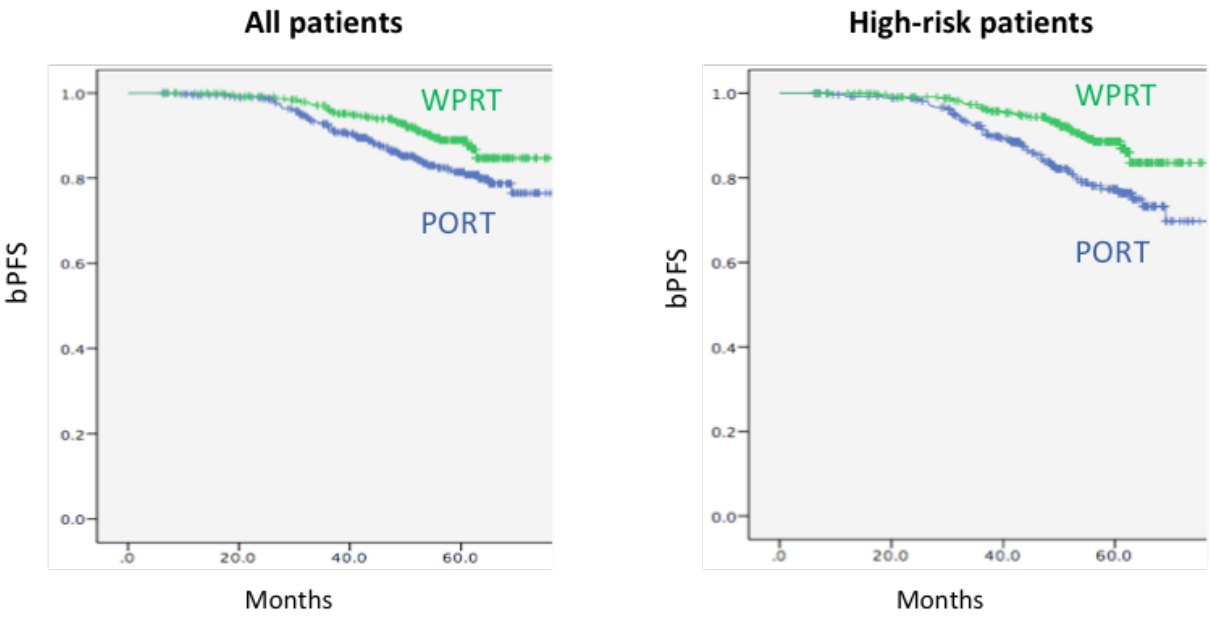

Figure 7.1. Kaplan-Meier bPFS curves of intermediate and high-risk prostate cancer patients treated with EBRT and HDR brachytherapy comparing the outcomes of WPRT vs PORT in the overall population (left) and the high-risk cohort (right). WPRT, w*hole pelvis radiotherapy; PORT, prostate-only radiotherapy; bPFS, biochemical progression-free survival*

3.

Intensity modulated brachytherapy system for dynamic modulation of shielded catheters

Gabriel Famulari and Shirin A. Enger

McGill University, Canada

CONTEXT OF THE STUDY

Radiation sources conventionally used in brachytherapy provide radially symmetric dose distributions. Conventional brachytherapy often results in less than ideal tumour dose conformity due to the non-symmetrical shape of the tumours, resulting in dose spillage to radiation sensitive organs at risk (OARs). Healthy tissue radiation toxicity limits the optimal dose distributions inside the tumour, and associated side effects can negatively impact patient quality of life. Intensity modulated brachytherapy (IMBT) is a novel form of high dose rate (HDR) brachytherapy technique delivered through rotating metallic shields that can dynamically direct radiation away from healthy tissues, potentially reducing complications relative to conventional HDR brachytherapy techniques.

OVERVIEW OF THE ABSTRACT

The purpose of this work is to present AIMBrachy, a novel delivery system enabling IMBT (Figure 1). To modulate the angular intensity of the source, AIMBrachy combines a custom-made 169Yb source with thin platinum shields (maximum thickness of 0.8 mm) within the catheter. The delivery system can be offered as an upgrade add-on to any commercial afterloader. The universal template for needle placement ensures that the system can match the geometry of existing templates for various sites. The potential benefits of AIMBrachy were evaluated retrospectively for a prostate HDR brachytherapy case using RapidBrachyMCTPS, an in-house Monte Carlo treatment planning system for brachytherapy applications.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

The AIMBrachy prototype uses a rotating mechanism which dynamically controls the orientation of thin shields with rotational accuracy below 1°. The platinum shield can reduce the dose on the shielded side by 75% compared to the dose on the unshielded side at a radial distance of 1 cm from the source (Figure 2). For the same minimum dose to the hottest 90% of the planning target volume (PTV), the IMBT plan resulted in a reduction in the bladder D_{2cc}, rectum D_{2cc}, and urethral D_{10} by 22%, 30%, and 10%, respectively (Figure 3).

WHAT IMPACT COULD YOUR RESEARCH HAVE?

For many cancer sites, the optimal dose cannot be delivered to the tumour due to normal tissue toxicity. AIMBrachy will allow the possibility to escalate dose inside the tumour volume, improving the probability of cure, while being able to more effectively shield healthy tissues, leading to lower toxicity. In the case of prostate brachytherapy, AIMBrachy can reduce the dose given to the bladder, rectum and urethra to levels previously unachievable with conventional brachytherapy. The universal design and compatibility with commercial afterloaders will facilitate the translation of this technology into clinical application.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

There is increased interest in magnetic resonance imaging (MRI) for radiotherapy planning. MRI-guided brachytherapy is the new gold standard for brachytherapy treatment planning, providing excellent delineation of the tumour and surrounding tissue. The potential exists for improved dose prescription and reporting for the target volume. In addition, there is a possibility to identify subvolumes within the tumour. With superb soft-tissue contrast and reduced margins, the need to provide highly conformal dose distributions is rapidly expanding, especially for highly non-symmetrical target volumes. AIMBrachy can lead to dosimetric improvements of brachytherapy treatment plans and thus has the potential to improve patient outcomes with regard to local control, overall survival and quality of life.

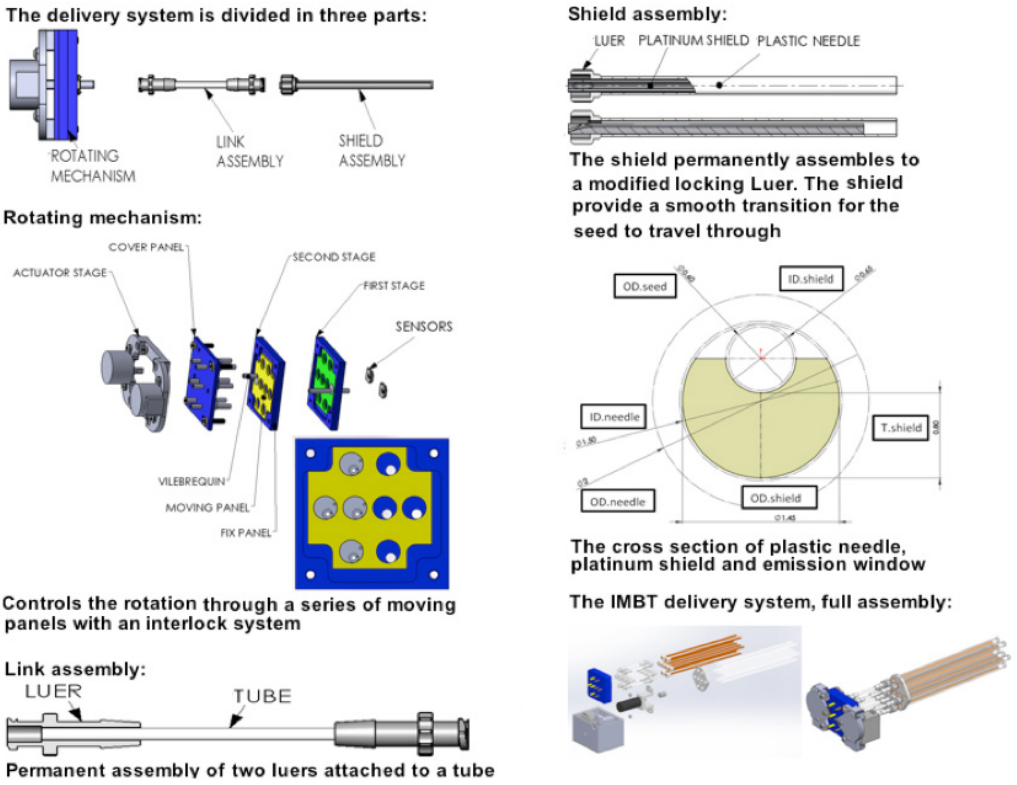

Figure 1. Schematic of the design of the AIMBrachy technology. The rotating mechanism, link assembly, and shield assembly are shown. Cross sections of the shielded catheter are displayed.

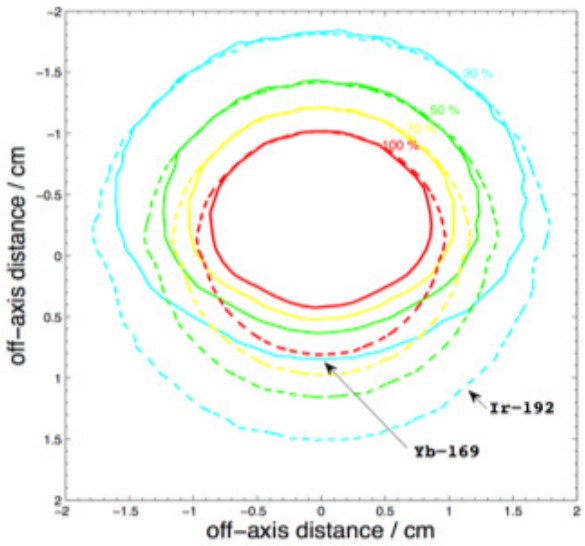

Figure 2. Isodose lines produced by ^{192}Ir and ^{169}Yb sources in combination with a platinum shield with a maximum thickness of 0.8 mm. The dose is normalized to the dose at a radial distance of 1 cm on the unshielded side.

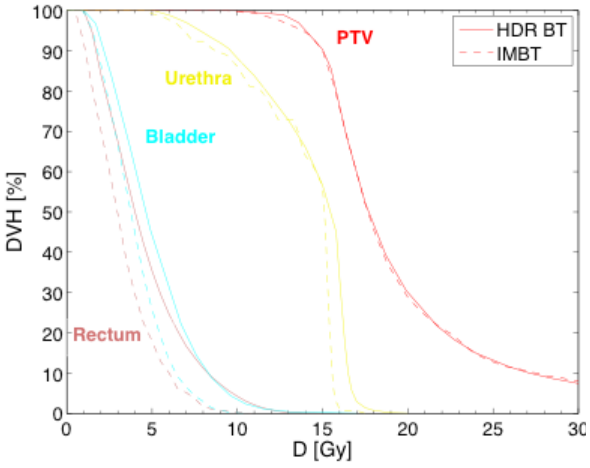

Figure 3. Dose-volume histogram (DVH) comparison between conventional high dose rate (HDR) brachytherapy and ^{169}Yb-based intensity modulated brachytherapy (IMBT) plans for a prostate cancer case.

4.

Risk factors for ureteral stricture after IGABT in cervical cancer: results from the EMBRACE studies

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CONTEXT OF THE STUDY

Standard treatment for locally advanced cervical cancer (LACC) comprises external beam radiotherapy, concomitant Cisplatin chemotherapy and 3D image guided adaptive brachytherapy (IGABT). Ureteral stricture is a rare but well known complication of pelvic radiotherapy. Ureteral strictures related to radiotherapy are often diagnosed at a late stage and the consequences range from asymptomatic organ dilatation, to loss of renal function and potential life threatening urosepsis.

With the introduction of IGABT in LACC, the dose to the tumour has been increased in many centres. Moreover, interstitial needles have been introduced as part of the treatment. Due to the close proximity of the ureters to the cervix, it has been postulated that IGABT may result in more ureteral strictures. The present study aims to provide a descriptive analysis and identify predictive factors for ureteral stricture in a large multicentre population treated for LACC.

OVERVIEW OF THE ABSTRACT

This is a multicentre study with a total of 1860 patients treated for LACC with IGABT in the retroEMBRACE and EMBRACE studies. Treatment consisted of external beam radiotherapy (45-50 Gy in 25-30 fractions) with concomitant Cisplatin chemotherapy given to 88.9% of the patients. IGABT was delivered with HDR BT (58.0%) or PDR BT (42.0%). Combined intracavitary/interstitial technique was used in 36.0% of patients. Severe to life threatening (grade 3-4) ureteral strictures were analysed with descriptive statistics. Predictive factors for ureteral stricture were analysed by univariate and multivariate statistics.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

At a median follow up of 34 (2-163) months, 38 patients were diagnosed with grade 3-4 ureteral stricture. The actuarial 3/5-year risk was 2.1%/2.5% for all patients. Advanced tumour stage T3-4 ($p=0.04$) and hydronephrosis at diagnosis ($p\leq0.001$) were the only significant risk factors identified. Patients with stage T1 (n=359) and T2 (n=1085) had a low risk of ureteral stricture (0.4%/1.0% and 1.1%/1.1% at 3/5 years, respectively). Patients with T3-T4 without hydronephrosis at diagnosis (n=274) had a 3/5 year risk of 2.6%/5.2%, compared to 13.9%/13.9% in patients with T3-T4 and baseline hydronephrosis (n=142) (see figure 1).

WHAT IMPACT COULD YOUR RESEARCH HAVE?

The study shows that severe to life threatening ureteral strictures rarely occurred in patients with small tumours (T1-2 tumours). The risk for ureteral stricture was significantly increased in patients with T3-T4 tumours, especially if hydronephrosis was present at diagnosis.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

Improvements in radiotherapy have resulted in increased cure rates. However, more patients are at increased risk for late morbidity after treatment. As a consequence, more studies have been focusing on late morbidity during the last decade. The present study is a part of this trend and apart from describing the risk for severe to life threatening ureteral stricture, the study also identifies the group of patients that have the highest risk for ureteral stricture. These results are invaluable for future radiotherapy of LACC for several reasons. First, the results can be used to inform patients about the risk for late morbidity after radiotherapy. Second, the results can be used to identify those patients that might benefit from increased surveillance and as a guide for future improvements in radiotherapy.

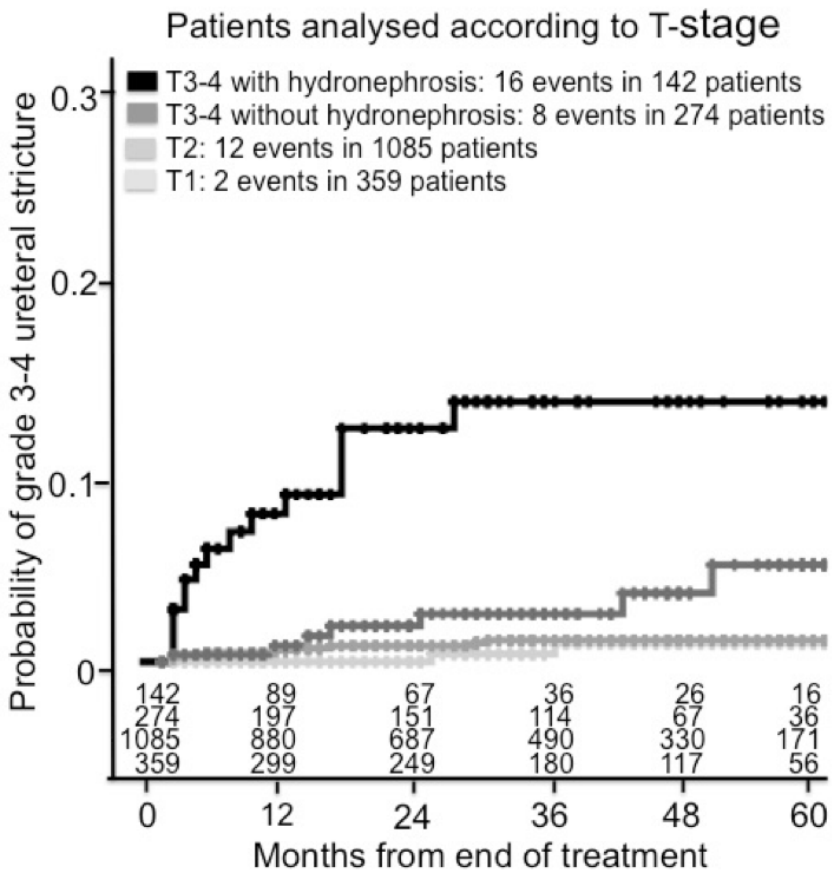
Patients analysed according to T-stage
T3-4 with hydronephrosis: 16 events in 142 patients
T3-4 without hydronephrosis: 8 events in 274 patients
T2: 12 events in 1085 patients
T1: 2 events in 359 patients
Probability of grade 3-4 ureteral stricture
0.3
0.2
0.1
0
142 89 67 36 26 16
274 197 151 114 67 36
1085 880 687 490 330 171
359 299 249 180 117 56
0 12 24 36 48 60
Months from end of treatment

Figure 1.

5.

QOL after APBI (multicatheter brachytherapy) versus WBI: 5-year results, phase 3 GEC-ESTRO trial

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CONTEXT OF THE STUDY

Accelerated partial breast irradiation (APBI) is an alternative procedure to conventional whole breast irradiation (WBI) and has been offered to selected, low-risk breast cancer patients after breast-conserving surgery (BCS) in several clinical trials. Several studies using multicatheter interstitial brachytherapy for APBI have reported promising outcomes. The GEC-ESTRO trial was the first prospective, randomised, phase 3 trial on this issue and showed that APBI using multicatheters is not inferior to WBI in patients with early breast cancer regarding local control and survival. To date, only few studies, mostly with small patient numbers and without randomisation, investigated quality of life (QoL) of breast cancer patients treated with APBI in comparison to WBI.

OVERVIEW OF THE ABSTRACT

In the phase 3 GEC-ESTRO trial comprising 16 European departments, patients with early breast cancer after BCS were randomly assigned to receive either WBI or APBI using multicatheters (2004 – 2009). 633 patients received APBI and 551 patients WBI. The primary endpoint of the trial was ipsilateral local recurrence. Now, we present 5-year results on QoL as one of the secondary end-points. QoL questionnaires (EORTC QLQ-C30, breast cancer module QLQ-BR23) were completed before radiotherapy (baseline 1), immediately after radiation (baseline 2), and during follow-up.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

- The share of available questionnaires at baseline 1 were 52·8% (n=334) after APBI and 57·0 % (n=314) after WBI, and stayed similar during follow-up.
- General health status was stable in both groups (range 0 to 100): baseline 1: APBI mean 65·5, SD 20·6 vs. WBI 64·6, SD 19·6 (p=0·37); 5 years: APBI 66·2, SD 22·2 vs. WBI 66·1, SD 21·8 (p=0·94).
- The only moderate, yet significant difference (difference of 10-20 points) between the groups was found in the breast symptoms scale. Breast symptoms were significantly more pronounced after WBI than after APBI at baseline 2 (difference of means 13·6; 95% CI 9·7 to 17·4; p<0·0001) and at 3-month follow-up (difference of means 12·6; 95% CI 9·6 to 15·5; p<0·0001).

WHAT IMPACT COULD YOUR RESEARCH HAVE?

Multicatheter brachytherapy-based APBI is a well-tolerated procedure that does not lead to a deterioration of QoL compared to WBI. This finding supports the use as an alternative treatment option after BCS in early breast cancer. An analysis of 10-year follow-up data of this study will be necessary to evaluate QoL taking into account late side-effects. To our knowledge, this trial is the largest series to date that reports on QoL after APBI vs. WBI. Presenting QLQ-mean values of >600 patients at baseline, this work might also prove as useful groundwork for future QoL studies concerning any kind of adjuvant breast irradiation. However, the proportion of available questionnaires was modest. The use of electronic QoL assessment could lead to more available data in future studies.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

This research reflects a growing awareness of effects of radiotherapy on QoL. In the management of early breast cancer with high survival rates and good local control the side effects of treatment as well as its impact on QoL should be as minimal as possible. As APBI presents a more focused form of radiation and constitutes an abbreviated course of therapy, this treatment approach could be more convenient for patients and will play a role in the management of early breast cancer. In view of ongoing studies investigating even more hypofractionated WBI with ever shorter treatment duration, it is essential that these techniques also prove to be similar regarding QoL.

RTT (Radiation TherapisT)

INTRODUCTION

FILIPE CIDADE DE MOURA

ESTRO 37: more than a meeting, a world of radiotherapy at a glance

ESTRO 37 was about widening the perspective and opening new horizons whilst meeting and embracing the unexpected. In such a great environment, science and innovation walk side by side providing new insights on the state of the art on a global scale.

The ESTRO 37 RTT scientific programme was tailored to meet advanced practice in radiation oncology and to focus on the greatest achievements and the role of developments of radiation therapists over the last decades. The starting point was undoubtedly related to one of the radiation oncology hot topics of the moment: the integration of MR Imaging with a LINAC. The RTT Pre-Meeting Course on "Clinical implementation and use of MR imaging in external beam radiation therapy", provided knowledge on the current and future role of MR applications in radiation therapy, coupled with safe and effective implementation of this emerging modality, for both imaging for planning and treatment guidance.

The ESTRO 37 RTT track reflected important milestones in the various domains of radiation oncology from the RTT perspective, resulting in well balanced topics covering the patient centered approach, education and training, advanced planning and treatment approaches and integrating high technology adaptive solutions underpinning safety and minimal risk in the clinical environment.

From ESTRO 31 (in 2012) the RTT track final debate has been highly appreciated and recognised amongst the RTT community, attracting members from different spectra and backgrounds, to promote discussion about the roles and challenges of radiation oncology in practice. Last year the debate focussed on advanced planning, "Where are we and, where are we going?"; this year the final debate was designed to reflect the new reality of growing technology and artificial intelligence with a controversial topic on *Autoplanning, is there still a bright future for RTTs after automation?*

Submitted abstracts to the RTT track at the ESTRO conferences, have grown annually with 210 abstracts from 30 countries submitted in 2018. This year also saw 45 abstracts on a range of topics submitted from 13 countries outside of Europe.

The highly scored categories focussed mainly on topics related to adaptive RT, autoplanning, deformable registration and OARs avoidance, Imaging for planning, IGRT/SGRT and motion management. From the highly scored abstracts, the RTT Scientific Advisory Group selected the following three as reflecting the clinical and scientific development and innovation towards the safe optimization of techniques and procedures.

The first abstract from Johannesson *et al.* presents a very interesting phase II study (PROPER), emphasising the role of the radiotracer 68Ga-PSMA-PET in tailoring the pelvic nodes treatment approach by treating the patients presenting with positive pelvic lesions using a VMAT SIB technique. The results have shown that sequential VMAT can be delivered with adequate coverage to the prostate bed and pelvic nodes, maintaining OARs within an acceptable dose range.

The second abstract submitted by Bakker *et al.* reports the feasibility of Deep Learning Contouring (DLC) for the head and neck region. This treatment site is always a challenge for accurate OAR segmentation, which is significantly time consuming, particularly with small, irregular variable structures. By using a large dataset of 698 patients, 22 OARs were evaluated comparing the DLC model with the Atlas Based Atlas Auto-Segmentation (ABAS) method. Quantitative evaluation using the DICE coeficient and Average Distance (AD) demonstrated a significant improvement for automatic contouring of the majority of OARs in the head and neck region.

The third abstract from Russel *et al.* is a study on optical surface detection for breast cancer patients for positioning and precise treatment localisation. Three Cohorts were selected for analysis of the reliability of the Surface Guided RT (SGRT) approach, concluding that the implementation of the SGRT method, can improve the patient setup accuracy with significant reduction of patient displacement, concluding that skin mark-free breast setup is feasible, promoting, at the same time, body image satisfaction and reduction of psychological distress due to tattoos or temporary pen marks.

Filipe Cidade de Moura
Chair, Scientific advisory group (SAG) for Radiation Therapy

1.

Sequential VMAT planning of 68GaPSMA-PET and PSA guided radiotherapy of lymph nodes and prostate bed

V. Johannesson[1], E. Wieslander[1], E. Kjellen[1], E. Brun[1], U. Bitzen[2], T. Olsson[1], P. Höglund[3], P. Nilsson[1], A. Gunnlaugsson[1]

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OVERVIEW OF THE ABSTRACT

Today, most patients with recurring prostate cancer after surgery receive RT to the prostate bed only (usually 70Gy/7 weeks). In some of these patients there may be spread to the lymph nodes. We applied high-tech sequential treatment planning as part of a clinical trial (PROPER) to patients selected for lymph node irradiation identified by new diagnostic tools (Ga-PSMA-PET, PSA-monitoring). After the fifth week of radiotherapy to the prostate bed the patients were classified as either responders or non-responders. The latter group received an additional 50Gy to the lymph nodes (20Gy concomitantly and 30Gy with an abutting plan). We have developed a novel treatment planning technique to achieve this goal.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

According to our research high quality treatment plans can be produced with sequential composite volumetric-arc therapy (VMAT) planning of patients selected for nodal irradiation. This was achieved by using a so called base dose plan technique using VMAT. $EQD2_3$ based evaluation of treatment plans showed full compliance with all dose criteria to OARs and target volumes with the exception of slightly low doses to the lymph nodes. By using an $EQD2_3$ corrected base-plan during treatment planning further improvement in dose coverage was achieved.

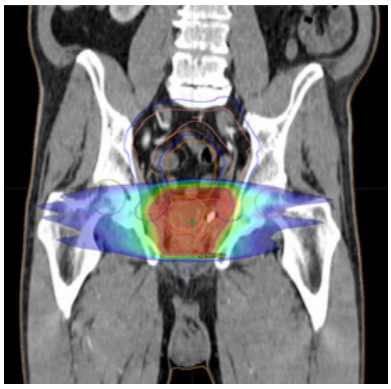
WHAT IMPACT COULD YOUR RESEARCH HAVE?

Development of personalized radiotherapy regimes for patients with recurrence after prostate surgery can improve outcome for these patients. This new way of planning selected patients sequentially with the help of $EQD2_3$ based correction of doses could improve the therapeutic index significantly. Further, the applied sequential treatment planning technique could be used for other indications.

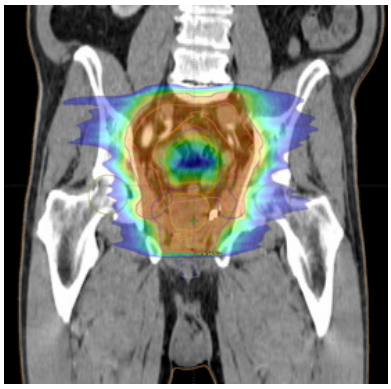
IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

The trend in radiation oncology is to personalize treatment with the aim to increase tumour cure with minimal morbidity. The fast technical development, e.g. diagnostic imaging, VMAT technique and planning systems, in recent years has made this possible.

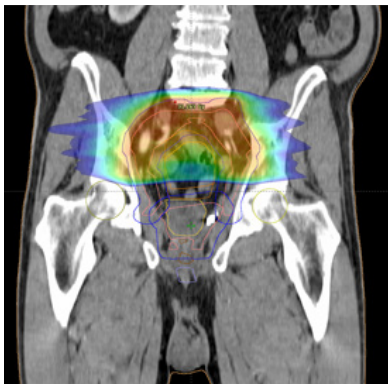
Sequential composite volumetric-arc therapy (VMAT) plans



Plan 1 – 50Gy/25fr

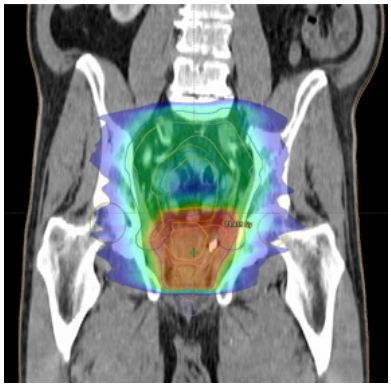


Plan 2 – 20Gy/10fr



Plan 3 – 30Gy/15fr

Sum of plans 1-3



Prostate bed 70Gy
Lymph nodes 50Gy

2.

Quantitative evaluation of deep learning contouring of head and neck organs at risk

Bakker H.[1], Peressutti D.[2], Aljabar P.[2], van Dijk L.V.[1], Van den Bosch L.[1], Gooding M.[2], Brouwer C.L.[1]

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CONTEXT OF THE STUDY

With ongoing developments in treatment technology (IMRT, VMAT) and image guided radiotherapy, it is becoming easier to avoid or reduce dose to the organs at risk (OARs). Therefore, as well as focusing on the target volume, attention can also be paid to normal/healthy tissue contoured as OARs. This is consistent with the aim in modern radiotherapy to minimize side effects, as well as to cure and control. Currently, semi-automated and manual contouring methods are in routine use. However, manual contouring in particular is time consuming and prone to inter-observer variability. Additionally, current methods for auto-contouring also require improvements and Deep Learning approaches are showing promise in this regard.

OVERVIEW OF THE ABSTRACT

The aim of this study was to compare the performance of Deep Learning Contouring (DLC) with Atlas-Based Auto-Segmentation (ABAS).

In total 22 OARs were manually contoured according to consensus delineation guidelines in a large set of H&N patients (n=698). These contours served as ground truth (where ground truth compares with the gold standard). Both auto-contouring methods were quantitatively compared against the ground truth by computing the Dice similarity coefficient (Dice) and Average Distance (AD).

The Dice coefficient measures the similarity of a pair of contours, where a value of one stands for perfect overlap. AD measures the mean closest distance of the automatically generated contour to the corresponding manual contour, averaged over all contour points.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

DLC provided a large number of OARs with relatively high Dice scores and low AD values [see Table 1 and Figure 1]. DLC outperformed ABAS for 17 out of 22 OARs.

- Small and/or elongated OARs, such as the arytenoids (median Dice left: DLC 0.60 and ABAS 0.16), carotids (median Dice left: DLC 0.73 and ABAS 0.36) and pharynx constrictor muscles (median Dice: DLC 0.70 and ABAS 0.62) were contoured more accurately with DLC.
- OARs with high anatomical variability, such as the parotids (median Dice left: DLC 0.85 and ABAS 0.79) and submandibular glands (median Dice left: DLC 0.80 and ABAS 0.69) were contoured more accurately with DLC.
- DLC performance was comparable with ABAS for the cerebrum, cerebellum, brainstem and oral cavity.

WHAT IMPACT COULD YOUR RESEARCH HAVE?

Generally, DLC results in contours closer to the ground truth than ABAS.

The work-load required to adjust automatic contours, if necessary, should therefore decrease. The introduction of DLC should therefore lead to time savings. When routine structures are auto-contoured, the time saved could be used to focus on contouring more difficult structures that might not be routinely contoured, or that may have an associated clinical outcome or side-effect.

This study supports the introduction of DLC in clinical practice. Furthermore quantitatively high quality auto-contouring provides an opportunity to reduce contouring variability within and between treatment centers. With DLC, more centers would be able to contour a larger number of OARs within consensus guidelines. Reducing dose to these OARs will result in better sparing of OARs and improved quality of life.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

There is much hype surrounding Artificial Intelligence in healthcare, but few tangible examples in radiotherapy where it is actually useful. The use of techniques from AI/DL makes it possible to learn rich and complex models from training data embodied by expertly contoured images. It is now becoming possible to apply DL models to tasks that are typically performed by trained human experts. With existing routinely contoured OARs being automatically contoured, we may be able to consider contouring more structures allowing the introduction of more sophisticated plans and furthering the personalization of treatment.

	Dice				AD (mm)			
	ABAS		DLC		ABAS		DLC	
	Med	IQR	Med	IQR	Med	IQR	Med	IQR
A Carotid L	0.36	0.20	0.73	0.13	4.16	2.69	1.32	0.90
A Carotid R	0.25	0.17	0.72	0.14	9.16	7.69	1.51	1.57
Arytenoid L	0.16	0.17	0.60	0.20	3.25	2.29	1.33	0.92
Arytenoid R	0.18	0.21	0.57	0.13	3.05	1.90	1.34	0.69
Brain stem	0.87	0.04	0.87	0.04	1.35	0.54	1.25	0.45
Buccal Mucosa L	0.72	0.11	0.77	0.06	1.81	0.82	1.33	0.46
Buccal Mucosa R	0.75	0.10	0.77	0.07	1.60	0.82	1.35	0.51
Cerebellum	0.94	0.03	0.94	0.03	1.14	0.60	1.13	0.47
Cerebrum	0.98	0.02	0.98	0.01	0.67	0.43	0.72	0.31
Crico	0.48	0.24	0.73	0.11	2.86	2.44	1.51	0.81
Esophagus	0.55	0.35	0.84	0.10	2.54	2.89	0.71	0.43
Glottic Area	0.51	0.21	0.74	0.10	2.26	1.67	1.04	0.50
Mandible	0.93	0.04	0.95	0.02	0.49	0.32	0.36	0.11
Oral Cavity	0.91	0.04	0.91	0.04	1.47	0.54	1.33	0.38
Parotid L	0.79	0.08	0.85	0.05	2.35	0.93	1.44	0.59
Parotid R	0.78	0.09	0.83	0.06	2.44	1.31	1.46	0.58
Pharynx	0.62	0.11	0.70	0.07	1.94	0.72	1.26	0.38
Spinal Cord	0.95	0.03	0.93	0.04	0.34	0.28	0.41	0.20
Submandibular L	0.69	0.10	0.80	0.10	2.08	0.86	1.44	0.81
Submandibular R	0.68	0.13	0.80	0.07	2.25	0.96	1.32	0.64
Supraglottic	0.71	0.14	0.80	0.08	1.74	1.16	1.12	0.61
Thyroid	0.61	0.23	0.85	0.06	2.57	1.84	0.93	0.40

Table 1. Quantitative results of contouring accuracy of ABAS (n=109) and DLC (n=109). Median and inter-quartile ranges are shown for Dice and average contour distance. Shaded cells highlight a statistically significant better performance (Mann-Whitney U-test, p<0.01).

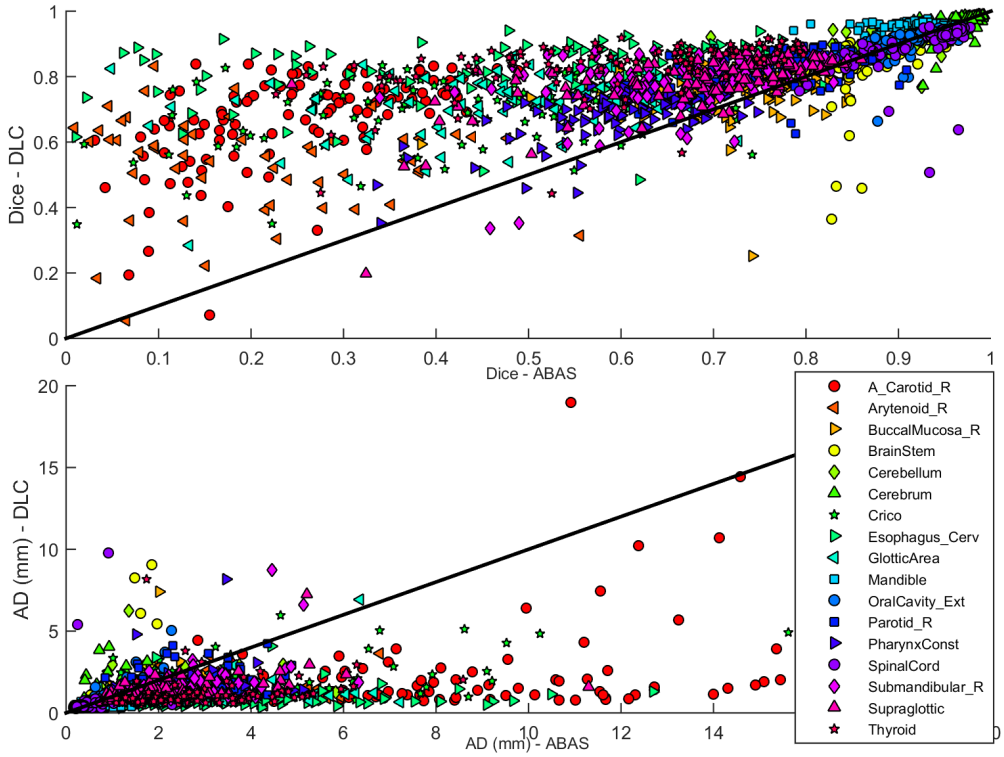


Figure 1.

3.

Surface guided radiation therapy for breast cancer improves accuracy without the need for skin marks

Catherine Russell, Hayley Mack, Sandra Paul, Sasha Senthi

Alfred Health Radiation Oncology, Melbourne, Australia

CONTEXT OF THE STUDY

Surface guided radiation therapy (SGRT) with AlignRT® (VisionRT, London) uses a speckled light pattern projected onto the patient. The light patterns recorded on high-definition camera from simulations are compared to those at treatment and differences from those expected and those measured are translated into real-time translational and rotational shifts, allowing adjustment of patient setup. Most centres that use SGRT do so in conjunction with skin marking. There is little published data on the accuracy of SGRT as the sole patient setup method.

OVERVIEW OF THE ABSTRACT

Alfred Health Radiation Oncology (AHRO) has been using SGRT in conjunction with skin marking to set up breast patients since 2009. In 2017 we began using SGRT alone for breast setup, in conjunction with daily verification imaging. This retrospective study evaluated initial setup accuracy of three cohorts: patients set up using 1) skin marking alone, 2) SGRT and skin marks, and 3) SGRT alone. Daily verification images were assessed for translational displacement from the planned position and an absolute displacement for each patient and fraction calculated.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

The most accurate setup was achieved using SGRT alone. The mean [standard deviation] absolute displacement was 0.27cm [±0.08cm].

SGRT with skin marks resulted in a mean absolute displacement of 0.28cm [±0.09cm].

Skin marks alone resulted in a mean absolute displacement of 0.39cm [±0.11cm].

There was a statistically significant improvement in initial setup accuracy when using SGRT, compared to skin marks alone ($p=0.009$ and $p=0.003$ for Cohort 2 and 3 respectively). This reinforces the value of SGRT as an accurate setup tool for breast treatments.

There was no statistically significant difference between the setup accuracy of the SGRT patients with and without skin marking ($p=0.66$). This suggests that it is feasible to remove all skin marks without a loss in accuracy.

WHAT IMPACT COULD YOUR RESEARCH HAVE?

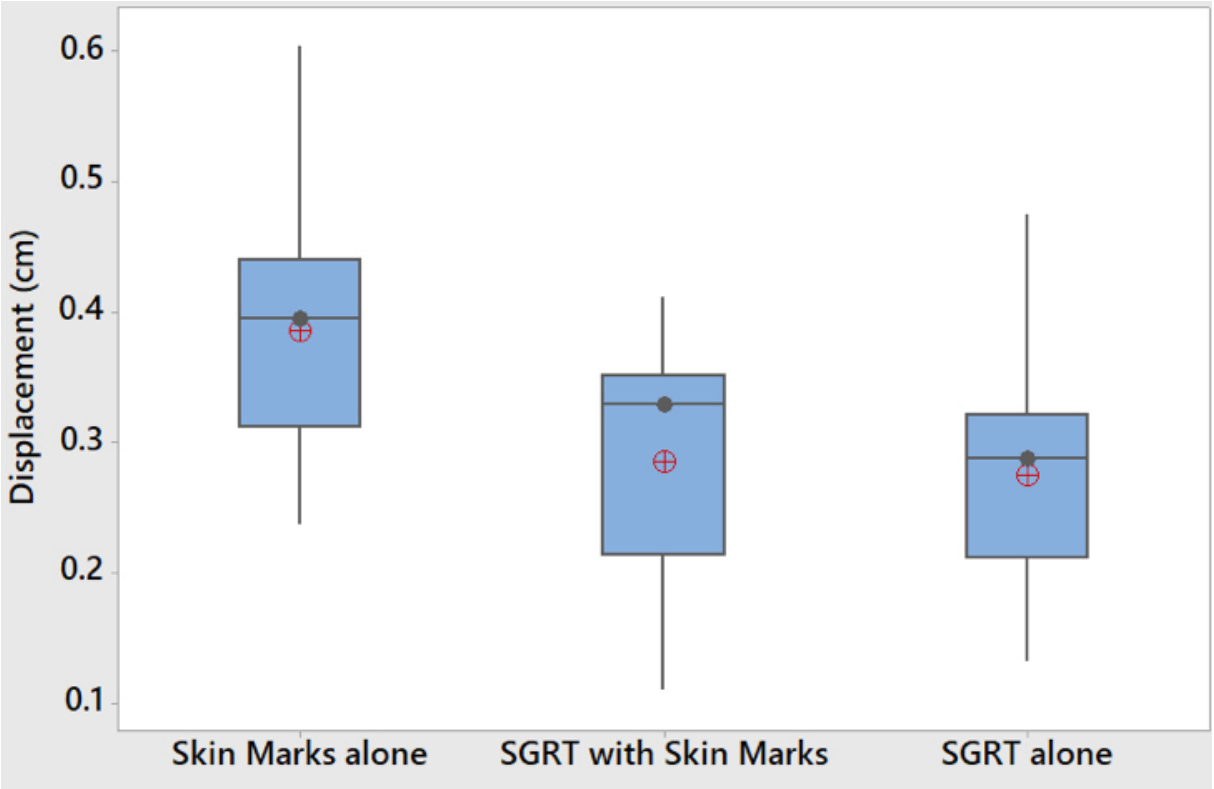
The ability to accurately set up patients without the need for tattoos or temporary skin markings has many benefits to both patients and clinicians. For breast patients especially, tattoos and skin marks may be in a visible area. There are documented psychosocial impacts of tattoos upon patients, as well as an infection control risk. Temporary skin marks require diligence to maintain and there is a risk of inaccuracies being introduced each time they are redrawn/reapplied. Adhesive tapes can also irritate skin.

The findings from this evaluation have led to further investigation into feasibility of markerless SGRT for other sites at AHRO.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

Cancer survivorship is becoming more prevalent and issues surrounding this—such as psychological impact of skin marks—are increasingly important.

We found that in a common radiotherapy technique, advances in SGRT technology—that are known to be efficient and less concerning for patients—also enable treatments which are at least as accurate as traditional techniques.


Displacement (cm)
0.6
0.5
0.4
0.3
0.2
0.1
Skin Marks alone
SGRT with Skin Marks
SGRT alone

RADIOBIOLOGY

INTRODUCTION

ANTHONY CHALMERS

There was a record number of Radiobiology abstract submissions to ESTRO 37 and the quality and diversity of research continues to increase in this crucial area of radiotherapy research.

Submissions this year highlighted very exciting pre-clinical work in the immuno-radiotherapy field. Some excellent studies evaluating immune biomarkers in clinical samples illustrate that clinicians and scientists are working together to help us understand how to apply the emerging knowledge in this area. This trend is also reflected in the number of clinical, radiobiological and interdisciplinary sessions that were devoted to immuno-radiotherapy at ESTRO 37.

As in previous years, the DNA damage response remained a hot topic and it was very encouraging to see novel molecular and genetic techniques being successfully applied in this increasingly complex field, as well as an increase in the repertoire of DDR inhibitors that are being evaluated.

Finally, the mechanisms by which cells die after exposure to radiation remain poorly understood so it was encouraging to receive high quality abstracts shedding light on this important topic.

In this congress report we share with you five reports based on abstracts that scored highly in the Radiobiology track of ESTRO 37.

I am sure that ESTRO 37 was an enjoyable and enriching experience!

Anthony Chalmers
Chair, Scientific advisory group (SAG) for Radiobiology

1.

CRISPR-Cas9 screen of DNA damage response reveals novel radiosensitisers for head and neck cancers

R. Dok1, M. Glorieux1, M. Bamps1, A. Sablina2, S. Nuyts3

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CONTEXT OF THE STUDY

The approval of the first PARP inhibitors for tumours harboring genetic defects in their DNA damage response (DDR) highlighted the importance of exploiting genetic deficiencies in DDR to improve the therapeutic index and paved the way for other DDR-targeted agents. Although increasing number of DDR-targeted agents are being tested as monotherapy in selected genetic backgrounds, it is likely that DDR agents ultimately will be used in combination with other DNA damaging agents such as radiotherapy to achieve a broader and more effective response. However, the knowledge of how to use DDR agents in combination settings is lagging behind the understanding of their use as monotherapy. Therefore, better understanding of the biology of the DDR in different cancers is required. As DNA repair in tumour cells is one of the important causes of therapy failure, this highlights the importance of assessing the radiosensitisation potential of targeted DDR agents.

OVERVIEW OF THE ABSTRACT

Targeted inhibition of the DDR response in combination with radiotherapy has the potential to increase the therapeutic index and improve treatment response in locally advanced head and neck squamous cell carcinoma (HNSCC) patients treated with radiotherapy. We assessed several radiosensitising strategies by performing a CRISPR/CAS9 loss of function screen targeting different classes of DNA repair genes. We found that suppression of DNA repair pathways showed different radiotherapy responses in HPV-negative and HPV-positive HNSCC cells. We validated the screen results by using DDR inhibitors in combination with radiotherapy in several preclinical models, including primary and recurrent patient-derived xenograft (PDX) models.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

We used a CRISPR-Cas9 loss of function screen and found that inhibition of base excision repair (BER) resulted in a better radiotherapy response in HPV-positive HNSCC, whereas inhibition of nucleotide excision repair had a more profound effect in HPV-negative HNSCC.

We found that HPV-positive HNSCC (samples from TCGA Biospecimen Metadata) showed higher expression of BER related genes compared to HPV-negative HNSCC.
We found that inhibition of non-homologous end-joining (NHEJ) showed a strong sensitising potential in both groups.

WHAT IMPACT COULD YOUR RESEARCH HAVE?

By making use of a CRISPR-cas9 library, we targeted different classes of DNA repair genes. We believe that extensive studies investigating the DDR and radiotherapy response using novel genetic and molecular technologies will result in a broader understanding of the biology of the tumours. This will lead to better understanding of the radiotherapy response and novel radiosensitising strategies, which can improve survival of cancer patients. This kind of research also highlights one of the major challenges for preclinical assessment of novel radiosensitising strategies, which is the assessment of the therapeutic index of the combination strategies, which ideally requires immune competent mice models.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

Despite technical improvements made in radiation delivery and optimization of radiation schedules, up to 50% of locally advanced HNSCC patients are confronted with locoregional tumour relapse indicating the need for novel treatment strategies. In this study, we show the preclinical potential of targeted inhibition of DDR in combination with radiotherapy for different groups of HNSCC. Moreover, we demonstrate that inhibition of DDR differentially affects the radiation response in HPV-negative and HPV-positive HNSCC, highlighting the importance of stratifying patients for optimal treatment options. This is especially important with the increasing number of DDR inhibitors entering clinical trials.

2.

Targeting PARP1 and the intra-S/G2 checkpoints for highly effective radiosensitisation of HPV+ HNSCC

T. Rieckmann[1,2], C.J. Busch[2], K. Hintelmann[1,2], Thomas Berenz[1,2], M. Kriegs[1], A. Münscher[2], C. Petersen[3], K. Rothkamm[1]

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CONTEXT OF THE STUDY / PRELIMINARY INFORMATION

In many countries the incidence of classical head and neck squamous cell carcinoma (HNSCC) is declining due to reduced tobacco and alcohol consumption. In contrast, the incidence of HPV-induced HNSCC, mostly localized to the oropharynx, is rising in many countries especially in the western world. Patients with HPV-positive HNSCC have a clearly favourable prognosis but the high cure rates currently come at the cost of aggressive multimodal treatment causing severe early and also irreversible late adverse events. Therefore, a number of deintensification trials have been initiated which are mostly based on the replacement of cisplatin by cetuximab or on de-escalated radio(chemo)therapy after induction chemotherapy or upfront transoral surgery. Molecular targeting approaches that take into account the special characteristics of HPV-positive HNSCC have not been implemented so far.

OVERVIEW OF THE ABSTRACT

HPV-positive HNSCC and cell lines derived thereof are characterized by an enhanced radiation sensitivity. We and others have previously shown that for the latter the enhanced sensitivity is based on a defect in DNA double-strand break repair and is associated with a profound and prolonged arrest in G2.We have further shown that individual inhibition of PARP1 as well as the intra-S/G2 checkpoints results in radiosensitisation. Here we wanted to test whether these approaches can be combined to achieve a more effective but still tumour-specific sensitisation that may be exploited in deintensification strategies.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

- The combined inhibition of PARP1 and the intra-S/G2 checkpoint (through Wee1/Chk1 inhibition) results in highly effective radiosensitisation of HPV+ HNSCC cells (mean dose enhancement ratio at 25% survival: 2).
- This radiosensitisation depends on S- and G2-phase cells since the mechanisms comprise the induction of severe replication stress and replication-associated DNA double-strand breaks as well as the inhibition of the subsequent compensatory G2-arrest.
- In line with these mechanisms, normal human fibroblasts, as an example of p53-proficient normal tissue cells, are only mildly radiosensitised, which suggests good tumour specificity.

WHAT IMPACT COULD YOUR RESEARCH HAVE?

The highly effective and tumour cell-specific radiosensitisation strongly suggests that this dual targeting approach may allow not only for the substitution of chemotherapy but also for a meaningful reduction of radiation dose in deintensified therapeutic regimes. This dual targeting strategy may be suitable in the primary as well as in the adjuvant setting following transoral surgery or induction chemotherapy.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

With a rapidly growing number of molecular targeted therapeutics becoming available and large efforts being made to identify targetable tumour alterations, precision oncology paves the way for personalized radiosensitisation strategies, which target specific pathways such as the DNA damage response or DNA repair.

HPV-driven tumours may represent an especially suitable entity for molecular targeted radiosensitisation, firstly, because HPV-positive HNSCC cells show an intrinsic DNA double-strand break repair defect and, secondly, because their transformation is mediated by the viral oncoproteins E6 and E7, which limit inter- and intratumoural heterogeneity. The molecular targeting of the remaining DNA damage response functions in these tumours should effectively and selectively radiosensitise most HPV-positive HNSCC (and possibly also HPV-positive anogenital tumours) and thus enable therapy de-intensification.

3.

Role of GDNF in the modulation of salivary gland stem cells (SGSCs) radiation response; regeneration or senescence?

Xiaohong Peng[1], Kärt Varendi[2], Peter W. Nagle[1], Lara Barazzuol[1], Cecilia Rocchi[1], Martti Maimets[1,3], Alejandra Hernandez Segura[4], Thijmen van Vliet[4], Marco Demaria[4], Jaan-Olle Andressoo[2], Rob P. Coppes[1]

[1]Departments of Cell Biology and Radiation Oncology, University Medical Center Groningen, University of Groningen, The Netherlands; [2]Institute of Biotechnology, University of Helsinki, Finland; [3]BRIC-Biotech Research and Innovation Centre, Copenhagen, Denmark; [4]ERIBA, University Medical Center Groningen, University of Groningen, The Netherlands

CONTEXT OF THE STUDY

Dry mouth syndrome or xerostomia is a common radiation-induced side effect resulting from damage to salivary glands which severely affects the quality of life of cancer patients. Xerostomia is a multi-faceted syndrome which manifests in oral dryness and infections, dental caries, and difficulties with food mastication.

Currently no cure is available, therefore the main focus of treatment is on optimizing regenerative potential of the glands post-irradiation. This can potentially be achieved by delivering a lower dose to the salivary glands or excluding the salivary gland from the radiation field entirely, or via pharmacologic treatments such as amifostine or pilocarpine. If these methods are unsuccessful, only generally supportive measures such as drinking water, artificial saliva and special diets remain.

OVERVIEW OF THE ABSTRACT

Restoration of secretory function is a challenge for regenerative therapy of radiation damaged salivary glands. Stem cell therapy has been proposed to induce such a functional regeneration. It has been suggested that glial-cell-derived neurotrophic factor (GDNF) promotes survival of mice salivary gland stem cells (mSGSCs). GDNF-treatment in combination with stem cell-based regenerative therapy could represent a promising treatment for radiation-induced hyposalivation and consequential xerostomia. However, the role of GDNF in SGSC survival and proliferation after therapeutic irradiation is still undefined. The purpose of this study was to investigate the role of GDNF in the modulation of SGSC response to irradiation.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

- GDNF does not protect mSGSCs against irradiation but seems to promote mSGSCs proliferation through the GDNF-RET signaling pathway.
- GDNF content dynamically changes in dividing mSGSCs.
- IR-induced upregulation of GDNF may be involved in IR-induced senescence.

WHAT IMPACT COULD YOUR RESEARCH HAVE?

Xerostomia, is a common side effect of radiotherapy and many medications, and seen in patients who suffer from Sjögren's syndrome and diabetes, as well as being a common consequence of aging. Therefore, the development of therapies to help restore normal salivary gland function in patients suffering from xerostomia is of great clinical interest.

GDNF-treatment in combination with stemcell-based regenerative therapy could represent a promising treatment for radiation-induced hyposalivation and consequential xerostomia.

Modulation of the GDNF signaling pathway could be a potential therapeutic target to reduce IR-induced senescence and avoid radiation-induced xerostomia.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

Radiotherapy has been used to treat many human malignancies but often causes severe side effects which can affect the patient's quality of life. We are trying to find a therapy that can be easily administered, efficient, cost effective, and has the potential to improve the quality of life for cancer patients. Our finding demonstrate that high regulation of GDNF can promote cell proliferation after irradiation, while, on the other hand, an IR-induced increase of GDNF may be involved in cellular senescence within the ductal cell compartment where the progenitor populations are located. Head and neck cancer patients undergoing radiotherapy and suffering from xerostomia could potentially benefit from GDNF treatment and modulation of the GDNF signaling pathway.

4.

DNA replication stress due to long gene expression causes radioresistance in GBM stem cells

R Carruthers, SU Ahmed, K Strathdee, S Ramachandran, EM Hammond, AJ Chalmers

Institute of Cancer Sciences, University of Glasgow, UK

CONTEXT OF THE STUDY

Glioblastoma (GBM) is a lethal primary human brain tumour characterised by inevitable recurrence despite triple modality treatment with surgical resection, chemotherapy and radiotherapy, and is associated with a median survival of 12-14 months. Despite intensive research efforts it remains refractory to current oncological treatments such as radiotherapy and is a cancer of unmet need.

GBM is a paradigm for the cancer stem cell theory in solid tumours, which suggests that only a subpopulation of tumour cells (GBM stem-like cells, GSC) have the necessary proliferative capacity to initiate and drive tumour growth. GSC are recognised to be resistant to radiotherapy and chemotherapy, likely due to their upregulated DNA damage response (DDR) cellular machinery which efficiently repairs DNA damage inflicted by common cytotoxic oncological therapies. Current treatments would appear relatively effective in dealing with a proportion of GBM tumour cells, but leave the GSC population intact, resulting in the commonly observed clinical pattern of inevitable recurrence a few months after initial therapy. In order to improve patient outcomes from GBM it would therefore seem vital to develop a greater understanding of the underlying GSC DDR phenotype to facilitate new therapies which actively target this treatment resistant GSC population.

OVERVIEW OF THE ABSTRACT

We wished to discover the underlying cause of DDR upregulation in GSC and investigate whether any identified causative mechanisms could be exploited in order to provide potential candidate GSC targeted therapies and sensitise GSC to radiotherapy. Despite a decade of research since enhanced DNA repair was first documented in GSCs, the underlying mechanism has remained elusive, but a greater understanding of the GSC DNA repair phenotype may lead to important improvements in treatment for this tumour site.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

This study presents 3 novel and important findings with significant clinical relevance:

- The upregulated DNA repair mechanisms seen in GSC which are responsible for GSC radiation resistance are a result of elevated levels of DNA replication stress (RS).

RS is the presence of long single strands of DNA within the cell nucleus due to difficulties in S phase DNA replication. RS causes non-lethal DNA damage which stimulates DNA double strand break (DSB) repair pathways allowing efficient DNA repair following radiation.

- We provide evidence that RS is elevated in GSC due to replication transcription collisions occurring at long neural genes.
- Inhibition of the RS response via dual inhibition of DNA repair proteins ATR and PARP produces GSC specific cytotoxicity.

WHAT IMPACT COULD YOUR RESEARCH HAVE?

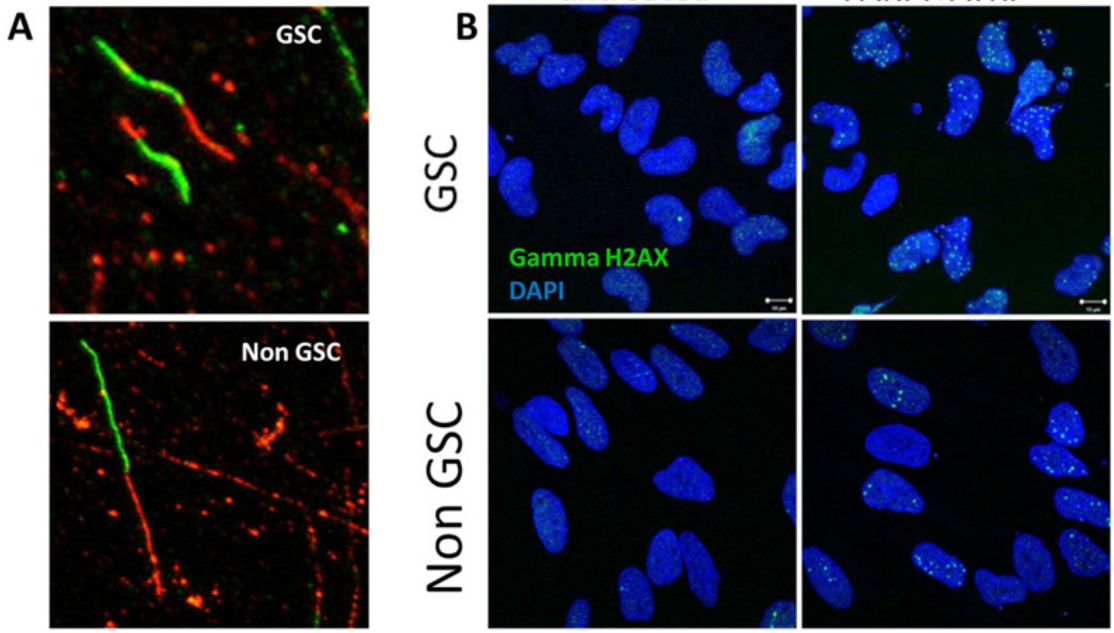
This study provides strong preclinical evidence to support trials of DDR inhibitor drugs in GBM, as a single modality and in combination with radiotherapy.

We describe RS as a novel radiation resistance mechanism in GSC, which may be relevant in cancer stem cells of other tumour sites.

We shed further light on the GSC phenotype and provide evidence that collisions between DNA transcription and replication machinery underlie the elevated RS seen in GSC. This phenomenon has been documented by other authors in neural progenitor cells, and our data therefore supports a neural progenitor cell of origin for GBM.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

RS has recently been described as a 'hallmark' of cancer and is a primary driver of genomic instability in multiple tumour types. Interest is growing in how RS and its associated multitude of cellular pathways could be harnessed to provide novel therapeutic approaches. RS is also an important phenomenon in normal (non malignant) embryonic stem cells, and causes the upregulated DDR seen in these cells. Furthermore, targeting of radiotherapy (and chemotherapy) resistant cancer stem cells is seen as an important priority for improving patient outcomes in treatment refractory tumours. Our research highlights the importance of RS in cancer stem cell biology, provides insight into a novel radioresistance mechanism and provides strong preclinical rationale for clinical trials of DDR inhibition in GBM.



A) GSCs exhibit elevated levels of DNA replication stress relative to non-GSCs as demonstrated by DNA fibre assay. DNA was extracted from GSC and non GSC *in vitro* following 20 minute incubation with thymidine analogues CIdU (green) and IdU (red). High power confocal microscopy images show representative elongating DNA fibres in GSC (top panel) and non-GSC (lower panel). DNA replication velocity is lower in GSC.

B) Representative confocal immunofluorescent microscopy images of gamma H2AX staining (a DNA double strand break marker) in GSC and non GSC under untreated (control) conditions and following a 48 hour exposure to inhibitors of the DNA repair proteins ATR and PARP. The combination of ATR and PARP inhibition induces DNA DSBs preferentially in GSC relative to non-GSC.

5.

Immune contexture in SCCHN and outcome after chemoradiotherapy in uni- and multicentric cohorts

J. Mueller-von der Gruen[1], F. Rödel[1], E. Fokas[1], I. Tinhofer[2], V. Budach[2], M. Krause[3], A. Linge[3], F. Lohaus[3], A. Sak4, M. Stuschke[4], A. Grosu[5], E. Gkika[5], A. Abdollahi[6], J. Debus[6], U. Ganswindt[7], C. Belka[7], S. Stangl[7], S. Pigorsch[7], G. Multhoff[7], S. Combs[7], S. Welz[8], D. Zips[8], M. Baumann[9], C. Rödel[1], P. Balermpas[1]

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CONTEXT OF THE STUDY

Squamous cell carcinoma of the head and neck (SCCHN) represents about 6% of the total cancer incidence and approximately 500,000 new cases are diagnosed each year worldwide [1]. Radical surgery including resection of the primary tumour and neck dissection of regional lymph nodes followed by postoperative chemoradiotherapy (CRT) or definitive CRT are both common treatment strategies for locally advanced SCCHN with a 5-year survival rate of 40-60% [2, 3]. The overall incidence of SCCHN is rising, especially in younger individuals due to the rising incidence in human papilloma virus (HPV)-infection-related oropharyngeal cancer [4]. The impact of immune cell infiltration on the prognosis of these tumours is becoming increasingly apparent [5, 6].

OVERVIEW OF THE ABSTRACT

The purpose of the underlying studies was to identify molecular markers with prognostic value that could serve both as predictors of outcome and as therapeutic targets. Therefore, we examined the prognostic value of tumour-infiltrating lymphocytes (TILs), tumour-associated macrophages (TAMs), CD56+ natural killer (NK) cells and the PD1/PD-L1 axis in patients with SCCHN in two cohorts treated with definitive or postoperative CRT. Furthermore, we correlated these findings with the expression of HPV/p16.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

The three main findings of our research on a definitively-treated cohort of 101 patients (median follow-up of 40 months) and an adjuvant cohort of 155 patients (median follow-up of 48 months) were as follows:

- High incidence of TILs (CD3+, CD8+) and NK cells (CD56+) correlated with significantly improved overall survival (OS), distant metastasis-free survival (DMFS), local failure-free survival and progression-free survival (PFS) (figures 1, 3).
- High incidence of TAMs (CD68+, CD163+) correlated with significantly impaired overall survival, distant metastasis-free survival and local failure-free survival for the definitively treated cohort. CD11+ myeloid cells were associated with cancer recurrence.
- High expression of TILs (CD3+, CD8+) and PD-1/PD-L1 was far more common in patients with positive HPV-status. Four different prognostic groups could be identified after examining the combined CD8/PDL1 expression (figures 2, 4).

WHAT IMPACT COULD YOUR RESEARCH HAVE?

TILs and NK-cells mediate tumour response to cancer treatments [7, 8]. The underlying studies show that CD8+ TILs and CD56+ NK-cells represent promising prognostic markers to identify SCCHN patients with a favorable clinical outcome after CRT. Our data underline that M2 TAMs impair outcome in cancer patients [9]. Furthermore, our data show that CD11b+ myeloid cells can be associated with tumour recurrences following CRT. PD-1 is the target of the already used inhibitors nivolumab and pembrolizumab [10-12] and based on that, we further highlighted the impact of the PD-1/PD-L1-axis on oncological outcome after CRT and could identify subgroups of patient that could particularly benefit from radioimmunotherapy. According to our findings, HPV/p16 positive tumours show an overexpression of these markers and should be considered immunogenic.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

Immune checkpoint targeting is already implemented in current cancer treatment strategies and its role is evolving towards personalized therapies [10-14]. The positive impact of host CD8+ cytotoxic TILs to radiation response has already been highlighted in recent preclinical reports of combinations of radiation and immune checkpoint inhibitors like PD-1/PDL1 axis [15-17]. Also, HPV-positivity affects the host response to the tumour, since HPV-positive tumours are generally more immunogenic [18, 19]. Future tumour assessment will therefore potentially include a set of routine markers i.e. p16, PD-1/PDL1, CD3, CD8 to estimate the tumours' response to immune therapy.

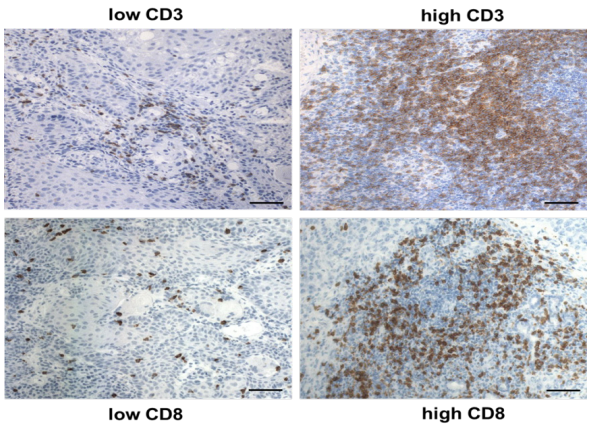

Figure 1. Immunostaining of TILs CD3 and CD8 expression

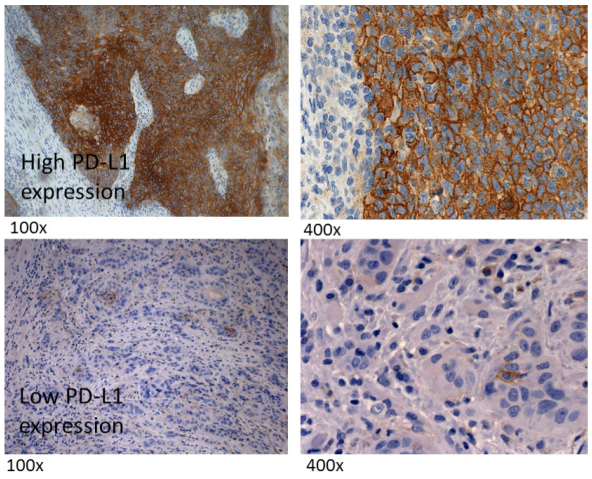

Figure 2. Immunostaining of PD-L1 expression

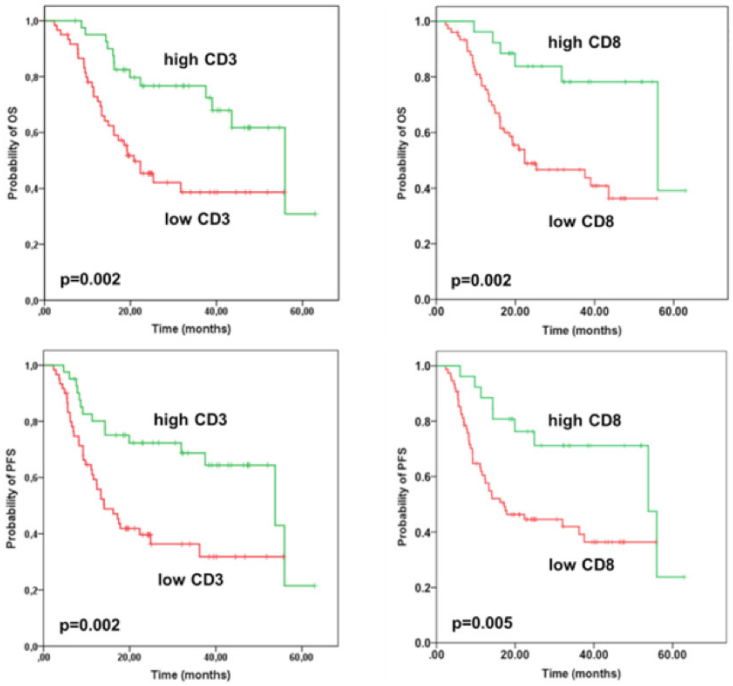

Figure 3. Prognostic role of TIL markers CD3 and CD8 regarding overall survival (OS) and progression-free survival (PFS) of patients with head and neck squamous cell carcinoma after definitive chemoradiotherapy.

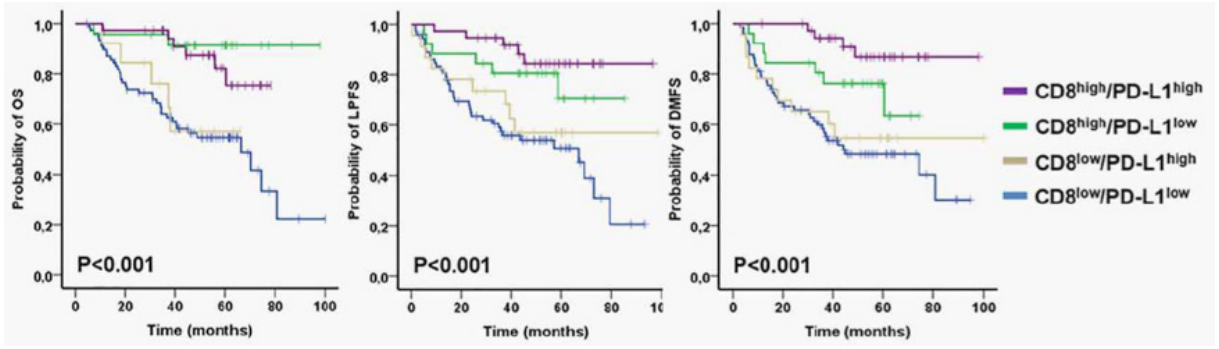

Figure 4. Overall survival (OS), local progression-free survival (LPFS) and distant metastasis-free survival (DMFS) according to combined CD8 and PD-1 status following adjuvant chemoradiotherapy. Green line = only CD8 positive; purple line = CD8 and PD-1 positive; yellow line = PD-1 positive; blue line = CD8 and PD-1 negative

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AWARDS GRANTED AT ESTRO 37

LIFETIME ACHIEVEMENT AWARDS

Rob Glynne-Jones (UK)
Michael Joiner (USA)
Richard Pötter (Austria)
David Thwaites (Australia)
Erik Van Limbergen (Belgium)

ESTRO AWARD LECTURES

Emmanuel van der Schueren award
The ESTRO School - Radiation oncology education of the highest standard for all
Christine Verfaillie (Belgium)

Donal Hollywood Award
Residual setup errors after image-guided radiation therapy (IGRT) are linked to overall survival in lung and oesophageal cancers
Corinne Johnson (UK)

Iridium Award
The dose rate effect in brachytherapy
Jean-Jacques Mazeron (France)

Klaas Breur Award
Biological precision in radiotherapy
Gillies McKenna (UK)

Jens Overgaard Legacy Award
This is not a target volume…
Vincent Grégoire (Belgium)

HONORARY MEMBER LECTURES

Imaging in oncology – let's shape the future together
Regina Beets-Tan (The Netherlands)

Sustaining radiotherapy services and development in low and middle-income countries
Soehartati Gondhowiardjo (Indonesia)

Radiotherapy of Hodgkin Lymphoma: revolutionary roots, challenging present, bright horizons
Joachim Yahalom (USA)

ACADEMIC AWARD

Jack Fowler University of Wisconsin Award
First clinical demonstration of online real-time liver tumor motion monitoring on a standard linac
Jenny Bertholet (Denmark)

COMPANY AWARDS

ESTRO-Elekta Brachytherapy Award
A predictive model for visual loss after uveal melanoma interventional radiotherapy (brachytherapy)
Luca Tagliaferri (Italy)

GEC-ESTRO Best Junior Presentation Sponsored by Elekta Brachytherapy
IBTR: second conservative radio-surgical treatment with interstitial BT HDR. From 2D to 3D planning
Chiara Cavallin (Italy)

ESTRO - Varian Award
Sub-pathologies and genomic classifier for individualised post-prostatectomy radiotherapy
Alejandro Berlin (Canada)

ESTRO - Accuray Award
Oxygen enhanced-MRI is feasible, repeatable and detects radiotherapy-induced non-small cell lung cancer (NSCLC) hypoxia changes
Ahmed Salem (UK)

BEST POSTER AWARDS

Radiation Oncologist
Low-dose radiation therapy as treatment for hand and knee osteoarthritis: two double-blinded RCTs
Michiel Minten (NL)

Physicist
Multi-centre evaluation of atlas-based and deep learning contouring using a modified Turing Test
Mark Gooding (UK)

Radiation TherapisT (RTT)
Stereotactic ablative RT with focal boosting in prostate cancer: feasibility on a 1.5 T MRI linac
Eline de Groot – van Breugel (NL)

ESTRO – ELSEVIER BEST POSTER AWARDS

The three ESTRO-Elsevier open access journals: ctRO (clinical), phiRO (physics) and tipsRO... also awarded the best poster in their category as follows:

ctRO
Radiation Oncologist
Implementing a novel online education programme to support RTQA – the EMBRACE-II experience
Simon Duke (UK)

phiRO
Physicist
Relationship of dose, FDG PET, CT lung response imaging, and radiation pneumonitis in NSCLC patients
Matthew La Fontaine (NL)

tipsRO
Radiation TherapisT (RTT)
The correlation between rotations of the pelvis and geometrical inaccuracy of the para-aortic region
Emina Ajanovic (NL)

Details on the best poster awardees will be presented in the July-August issue of the newsletter.

AWARDS

ON THE FOLLOWING PAGES YOU CAN FIND SUMMARIES OF REPORTS BY AUTHORS OF ABSTRACTS WHICH WERE SELECTED FOR SOME OF THE AWARD SESSIONS AT ESTRO 37.

ESTRO AWARD LECTURE

DONAL HOLLYWOOD AWARD

Residual setup errors after IGRT are linked to overall survival in lung and oesophageal cancers

Corinne Johnson, Gareth Price, Corinne Faivre-Finn and Marcel van Herk

Manchester Academic Health Science Centre, The University of Manchester, The Christie NHS Foundation Trust

CONTEXT OF THE STUDY

Radiotherapy treatment plans are bespoke, and meticulously created for each individual patient's anatomy and disease. During the course of radiotherapy, image guidance (IGRT) is often used to ensure that the patient position for each daily treatment is as close as possible to that in which they were planned. Many IGRT protocols utilise an action threshold. If the daily patient setup error (or shift) from their plan exceeds this action threshold then their position will be corrected. This means that when the action threshold is not met, the treatment will be delivered with small residual setup errors in the patient position. The treatment a patient actually receives, therefore, may differ to some extent from that which was prescribed. Our hypothesis was that these small differences in how a treatment is delivered may have an impact on patients' clinical outcomes.

OVERVIEW OF THE ABSTRACT

In this study we aimed to determine whether small residual setup errors that remain after an IGRT protocol has been applied are related to overall patient survival.

In a cohort of non-small cell lung cancer patients, we estimated the mean residual setup error over the whole course of treatment and the direction of this shift relative to the centre of the heart. We demonstrated that these residual errors were independent of other clinical parameters (they are truly random), yet that they are related to patients' overall survival. We validated our results in a cohort of oesophageal cancer patients.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

We found that patients with small residual shifts towards the heart have significantly worse overall survival than those who have residual shifts away from the heart. The size of the shift did not correlate with patient survival, suggesting it is the direction of the shift that is important. The same result was observed in the oesophageal cancer cohort. Our results provide the first direct evidence of the importance of ensuring correct patient positioning through the use of IGRT. They also highlight the significance of the heart, being more sensitive during thoracic radiotherapy than expected with early effects on survival.

WHAT IMPACT COULD YOUR RESEARCH HAVE?

Firstly, our work demonstrates the importance of accurate IGRT for thoracic radiotherapy. Secondly, this research suggests that simple changes in IGRT imaging protocols for thoracic tumour sites, such as increasing the imaging frequency and lowering the action threshold to reduce residual errors, can have a significant impact on overall patient survival. Finally, our findings, together with other contemporary work on the impact of cardiac dose on survival, also strongly suggest that stricter heart dose constraints should be put in place, and that doing so may reduce post-radiotherapy mortality.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

The analytical approach used in this work – the retrospective mining and analysis of large volumes routinely collected data – is a relatively recent and growing trend in scientific research and the medical sciences in particular. Observational studies of this nature are a complementary counterpart to gold standard randomised controlled trials and seek to address the concerns around their generalizability to the whole population. Furthermore, there is now widespread recognition that there are huge amounts of information about prognosis, radiotherapy quality and patient response captured in the images that each patient accumulates during their care pathway, and that careful analysis of these data can uncover important evidence for the efficacy of different treatments. Going forwards, we expect that data sharing approaches such as distributed learning will enable us to learn on larger and more detailed datasets, leading to evidence informing how best to deliver cancer therapy to individual patients.

UNIVERSITY AWARD

ESTRO-JACK FOWLER UNIVERSITY OF WISCONSIN AWARD

First clinical demonstration of online real-time liver tumor motion monitoring on a standard linac

Jenny Bertholet[1,2], Jakob Toftegaard[1], Rune Hansen[1], Esben Worm[1], Hanlin Wan[3], Parag Parikh[3], Britta Weber[1,4], Morten Høyer[1,4], Per Poulsen[1]

[1]*Aarhus University Hospital, Department of Oncology, Aarhus, Denmark.*
[2]*The Institute of Cancer Research and the Royal Marsden NHS Foundation Trust, Joint Department of Physics, London, UK.*
[3]*Washington University School of Medicine, Department of Radiation Oncology, St-Louis, USA.*
[4]*Danish Center for Particle Therapy, Aarhus, Denmark.*

CONTEXT OF THE STUDY

Respiratory motion is challenging for accurate radiotherapy delivery in the thorax and in the abdomen. Active motion mitigation (gating, tracking) may improve delivery accuracy but requires real-time target localization. Patients often have implanted radio-opaque markers, acting as surrogates for the tumour position, which can be detected by intra-fraction x-ray imaging. Currently commercially available methods on specialized accelerators combine an external surrogate with occasional stereoscopic x-ray imaging of implanted markers to obtain internal motion monitoring with high accuracy. This however, requires additional and costly hardware. As an alternative, Kilovoltage Intrafraction Monitoring (KIM), uses the gantry mounted x-ray imager of a standard linear accelerator to continuously image and detect the fiducial markers and estimate their 3D position. KIM, however, gives more imaging dose to the patient and it cannot be used for more complex treatments with couch rotations.

OVERVIEW OF THE ABSTRACT

In this study, we developed, validated and clinically demonstrated automatic tumour motion monitoring on a conventional linac by Combined Optical and Sparse Monoscopic Imaging with Kilovoltage x-rays (COSMIK). COSMIK combines external monitoring with automatic marker segmentation in x-ray images (figure 1a). The internal and external motion are related by an external correlation model (ECM). COSMIK was validated in experiments and simulations using known internal and external motion from 12 liver patients. In additional simulations, the accuracy of COSMIK was compared with that of KIM and with ECM with stereoscopic imaging (similar to the commercially available methods).

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

1. This study is the world's first clinical demonstration of online, real-time respiratory motion monitoring using only conventional equipment.
2. COSMIK is less accurate than KIM but similar to ECM with stereoscopic update (figure 1b) with a 3D root-mean-square error consistently below 2mm.
3. Despite somewhat lower accuracy, COSMIK offers important advantages over KIM such as reduced imaging dose, no loss in kV image quality by MV cross-scatter, compatibility with couch rotations, robustness against occasionally failed and rejected segmentations, and an uninterrupted position signal available throughout the treatment fraction for motion evaluation and prediction training.

WHAT IMPACT COULD YOUR RESEARCH HAVE?

Our research could have an impact on patient treatments very soon since it has been demonstrated clinically in this study. Using COSMIK, treatment could be adapted in real-time with gating or tracking on a conventional linac. There is also increased evidence that target rotation (in addition to translation) should be monitored and accounted for. This is possible with COSMIK since the position of each marker is monitored individually. The safety margins could be reduced resulting in better sparing of healthy tissues while maintaining or improving target coverage.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

Last year's ESTRO was marked by two main trends with particle therapy becoming more and more widespread and MR-guided radiotherapy becoming a clinical reality. While these technologies hold a great potential for high precision radiotherapy, they are also characterized by a high cost and will most likely not be available to every patient. The ESTRO 2020 vision is that each patient should have access to state of the art radiotherapy. Methods like COSMIK and KIM have the versatility, accessibility and low cost needed to make real-time adapted radiotherapy a standard of care in the near future.

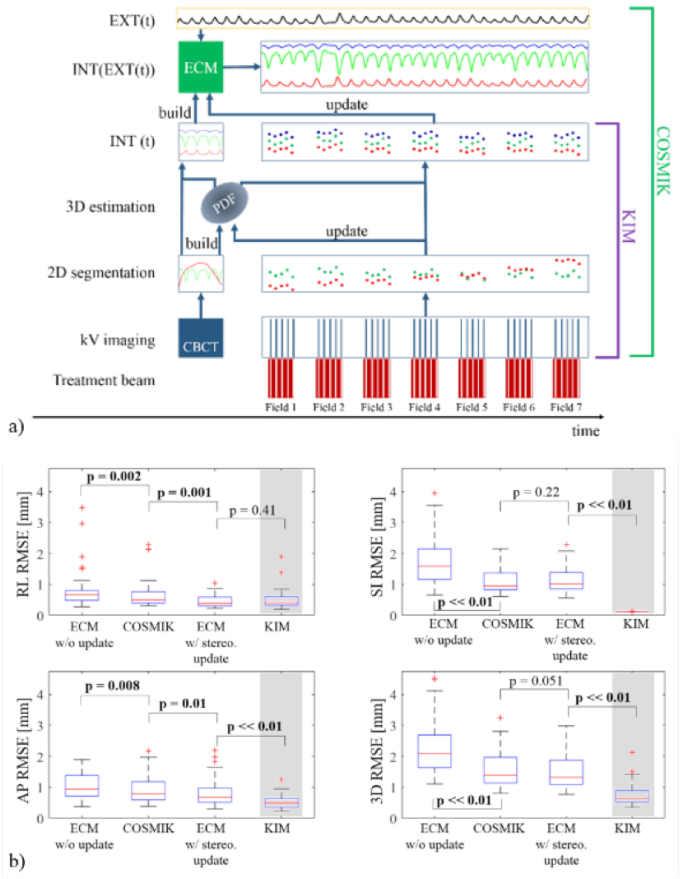

Figure 1: a) COSMIK workflow. The intra-treatment 3D position estimation by sparse kV imaging converges to the KIM workflow with increased imaging frequency. b) Boxplots of the root mean square errors (RMSE) along Right-Left (RL), Superior-Inferior (SI), Anterio-Posterior (AP) and in 3D for COSMIK, ECM with stereoscopic update and KIM. The error for ECM without update is shown for comparison. (Adapted from Bertholet et al. PMB (2018))

COMPANY AWARD

ESTRO-ACCURAY AWARD

Oxygen enhanced-MRI is feasible, repeatable and detects radiotherapy-induced NSCLC hypoxia changes

Ahmed Salem, Ross A. Little, Adam K. Featherstone, Susan Cheung, Yvonne Watson, Julian Matthews, Marie-Claude Asselin, Alan Jackson, Geoff J.M. Parker, Corinne Faivre-Finn & James P.B. O'Connor

University of Manchester/ The Christie NHS Foundation Trust, UK

CONTEXT OF THE STUDY

Hypoxia (oxygen deprivation in the tumour) is linked to poor radiotherapy response and survival in nearly all cancers including non-small cell lung cancer (NSCLC). For this reason, radiation oncologists have long been fascinated with therapies that target hypoxia in an attempt to improve cancer outcomes.

However, hypoxia-targeted therapies are only successful in selected patients (those with hypoxic tumours of course!). There is therefore a need to develop tests (biomarkers) that can be easily translated in the clinic to detect and track changes in tumour hypoxia. These biomarkers could then be utilised to select patients for future trials.

Oxygen-enhanced MRI (OE-MRI) is an exciting and novel imaging technique which uses oxygen as a contrast material. By applying a brief oxygen challenge while the patient is inside the scanner, we can measure change in proton longitudinal relaxation rate (R1) providing information on tissue oxygenation.

We can distinguish hypoxic tumour regions from regions with normal levels of oxygen (normoxic) if OE-MRI is then combined with dynamic contrast-enhanced MRI (DCE-MRI), which provides tumour blood flow information (FIGURE 1).

OVERVIEW OF THE ABSTRACT

The primary tumour of oesophageal cancer moves freely Our study was designed to enable the clinical translation of MRI biomarkers of hypoxia in NSCLC.

First, we wanted to assess safety, tolerability and feasibility of performing OE-MRI in NSCLC patients as this was the first OE-MRI study in NSCLC patients.

We then went on to determine the precision of MRI biomarkers of NSCLC hypoxia and their sensitivity to detect changes following radiotherapy to see whether these are useful biomarkers to take forward in the clinic.

In all, 23 NSCLC patients participated in this study.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

OE-MRI safety, tolerability and feasibility: We found that OE-MRI was safe and well-tolerated in NSCLC patients.

We were also excited to see that OE-MRI produced readily identifiable MRI signals in the aorta (aka input function). This provided first-in-man demonstration that this technique can be applied in the thorax using simple, patient compliant oxygen delivery using just a simple face mask. systems *(clinical translation)*; FIGURE 2A.

Precision of MRI biomarkers of hypoxia: The MRI biomarker perfused Oxy-R (hypoxic) volume (see Fig 1 for more info on how this was derived) showed excellent repeatability, consistently classifying and distinguishing hypoxic from normoxic NSCLC tumours *(technical validation)*; Fig 2B.

Post-radiotherapy changes: The MRI biomarker perfused Oxy-R (hypoxic) volume also reduced significantly following radiotherapy; Fig 2C.

Preclinical experiments in mice with lung tumours confirmed that changes in the MRI biomarker perfused Oxy-R were in fact related to tumour hypoxia *(biological validation)*.

In summary, our study shows that OE-MRI can IDENTIFY and TRACK changes in tumour hypoxia in patients with NSCLC.

WHAT IMPACT COULD YOUR RESEARCH HAVE?

I think the findings of this study support efforts to incorporate this biomarker in future biomarker-driven hypoxia-targeted therapy trials and radiotherapy dose intensification studies in NSCLC patients.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

Lung cancer is the leading cause of cancer death worldwide. The survival of lung cancer patients has changed little over the past 2 decades. This is especially true in locally-advanced NSCLC where a therapeutic plateau has been reached with standard (chemo)-radiotherapy. We need to improve outcomes of these patients.

Hypoxia, which is nearly exclusively restricted to cancer cells, represents an attractive therapeutic target and hypoxia-targeted treatments are likely to be associated with a favourable therapeutic ratio in locally-advanced NSCLC.

The development and validation of imaging biomarkers of hypoxia such as OE-MRI in our study will pave the way for biomarker-driven trials to investigate hypoxia-targeted therapies or radiotherapy dose intensification studies in the context of (chemo)-radiotherapy in NSCLC.

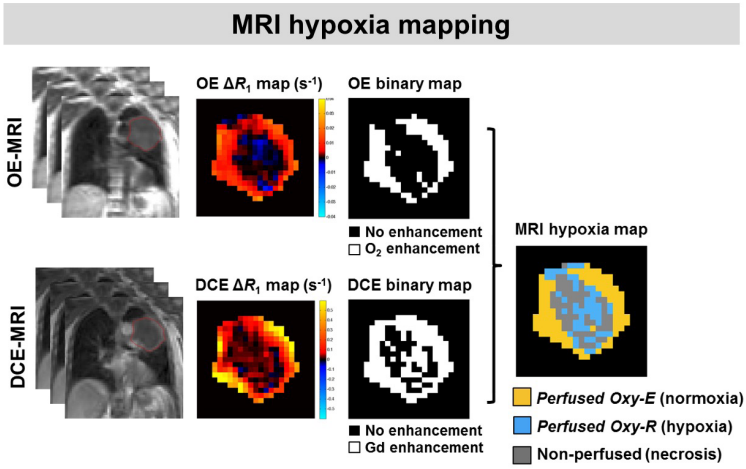

FIGURE 1: Quantitative OE-MRI and DCE-MRI tumour Δ*R*1 maps were binarized to distinguish *perfused Oxy-E* (normoxic), *perfused Oxy-R* (hypoxic) and non-perfused (necrotic) tumour regions

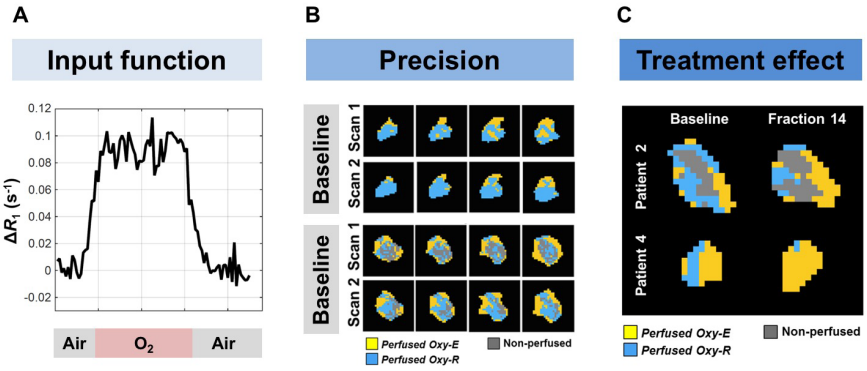

FIG 2: (A) Oxygen challenge resulted in a significant increase in measured R_1 in the aorta in all patients. This was reversed following switch back to air breathing; *input function* demonstrated

(B) MRI mapping of tumour hypoxia was spatially repeatable in tumour, nodal and distant metastatic lesions across a range of tumour and hypoxic volumes. All repeat scans were acquired before the start of radiotherapy

(C) There was a significant reduction in hypoxia, as measured by the MRI biomarker *perfused Oxy-R*, in 8 out of 12 patients following radiotherapy

COMPANY AWARD

ESTRO-VARIAN AWARD

varian

Subpathologies and genomic classifier for individualised post-prostatectomy radiotherapy

Alejandro Berlin[1], Melvin Chua[1], Hong Truong[2], Ali Hosni[1], Melania Pintilie[1], Elai Davicioni[3], Adam Dicker[2], Theo van der Kwast[4], Robert Bristow[1], Robert Den[2]

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[2]*Sidney Kimmel Medical College at Thomas Jefferson University, Department of Radiation Oncology. Philadelphia, USA.*
[3]*GenomeDx Biosciences, Inc. Vancouver, Canada.*
[4]*Department of Pathology and Laboratory Medicine, University Health Network. Toronto, Canada.*

CONTEXT OF THE STUDY

Patients that have undergone radical prostatectomy for localized prostate cancer and are considered at higher risk of disease recurrence (e.g. those with positive surgical margins) and those with evidence of disease recurrence (e.g. rising serum prostate-specific antigen [PSA]) are often treated with post-operative radiotherapy. Moreover, some men are offered the addition of hormonal therapy to their radiation treatment to increase their chances of cure.

However, current conventional clinicopathologic prognostic factors (e.g. pathological stage, Gleason score, margins status) are imprecise and account for only a fraction of inter-patient heterogeneity and responses to treatment, leading to significant over- and under-treatment of men in this setting. To date, no test robustly discerns patients unlikely to fail after local treatment due to the presence of occult distant disease, informing the optimal treatment intensification strategy.

OVERVIEW OF THE ABSTRACT

We aimed to determine the role of previously investigated biomarkers in curative-intent prostatectomy or radical radiotherapy (unfavorable subpathologies: intraductal carcinoma and cribriform architecture (IDC/CA), and a 22-gene genomic classifier [GC]), in a cohort of men treated with maximal local therapies (prostatectomy plus post-operative radiotherapy [PORT]). In this selected scenario, we found that both presence of pathological variants IDC/CA or an adverse GC score predicted for worse outcomes despite maximal local therapies, suggesting these biomarkers predominantly predict a higher-risk of distant spread. Therefore, we propose a judicious stepwise use of these two biomarkers for individualizing therapies (e.g. addition of hormonal therapy, investigational systemic treatment intensification) in this clinical conundrum.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

- IDC/CA were found in half of the patients, and did not correspond to high GC scores. This suggests IDC/CA and GC reflect independent aspects of the disease's biology and clinical behaviour.
- Both IDC/CA and high GC provided independent prognostic information after accounting for conventional clinicopathologic features. IDC/CA presence translated into a higher risk of biochemical failure and metastases (hazard ratio 2.5-3.1), while those with low GC scores had significantly lower risk of such events (hazard ratio 0.15-0.25).

WHAT IMPACT COULD YOUR RESEARCH HAVE?

- This study supports previous work and encourages the broader community to systematically ascertain presence of IDC/CA in prostate samples. Importantly, this is a biomarker that can be quantified in conventional routinely used H&E staining.
- Based on our results, a prospective biomarker-driven study could be proposed for treatment individualization in the post-prostatectomy setting. We envisage sequential IDC/CA and GC assessment to guide and individualize PORT and systemic treatment intensification approaches.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

This study is framed within the personalized cancer paradigm, in which molecular analyses of a tumour from each individual patient will provide guidance for the selection of the most effective therapies and thereby improve treatment outcomes. Our H&E staining-based evaluation of IDC/CA as a first step, aims to maximize readily available information for outcome prognostication. In the context of ever-rising costs and limited access to care, this is a widely applicable method for guiding treatment individualisation and value-enhancing practices.

Our study provides evidence and opens an opportunity to collaborate in a multi-centre biomarker-driven study in the post-prostatectomy setting. The overarching goal is to individualise treatment strategies based on novel tests, allowing us to provide best oncologic and quality-of-life results by utilising intensification strategies (e.g. hormonal therapy) only in those most likely to benefit from it.

COMPANY AWARD

ESTRO-ELEKTA BRACHYTHERAPY AWARD

A predictive model for visual loss after uveal melanoma interventional radiotherapy (brachytherapy)

L. Tagliaferri[1], M.M. Pagliara[2], J. Lenkowicz[1], R. Autorino[1], A. Scupola[2], M.A. Gambacorta[1], L. Azario[3], D. Giattini[2], V. Lancellotta[4], M. Ferioli[5], V. Valentini[1], M.A. Blasi[2].

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Department of Radiation Oncology – GEMELLI-ART (Advanced Radiation Therapy), Gemelli University Hospital - "Università Cattolica del Sacro Cuore" Rome, Italy

CONTEXT OF THE STUDY

Episcleral interventional radiotherapy (brachytherapy) is a reliable alternative to surgical enucleation for the treatment of small and medium-sized choroidal melanomas with excellent local control and survival rates. However, this treatment is not free from local toxicity and the benefits of eye preservation may be jeopardised by visual function impairment that can be related to numerous factors.

OVERVIEW OF THE ABSTRACT

The main purpose of this research was to develop a toxicity prediction tool (nomogram), taking advantage of a large database. This mathematical predictive prognostic model proved to be useful in clinical practice to identify patients that have a higher risk to develop visual function loss after Ruthenium-106 plaque Interventional Radiotherapy (brachytherapy) for uveal melanoma.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

The analysis of the characteristics of the tumour, together with treatment and patients' data allow development of a useful tool for the prediction of the percentage risk of toxicity for each patient. This prognostic model, matching the pre-treatment information, can identify patients that can potentiality develop visual function loss 3 years after the treatment. The tool is represented by a nomogram that can be easily used in daily clinical practice - so that the physician can modulate and personalize the treatment in order to achieve the best possible local control and survival with the best possible quality of life.

WHAT IMPACT COULD YOUR RESEARCH HAVE?

This research confirms that in modern oncology survival can be improved but highlights also the need to thoughtfully take into account all the consequences for the quality of life of our patients when deciding the treatment option, they will undergo. The use of a decision support system, such as the nomogram for determining the patient's visual prognosis, helps in identifying the best individually tailored treatment for each patient. Furthermore, this kind of tool can help the physician in identifying benefits for patients by applying an integrated multitherapy strategy considering all the neoadjuvant or adjuvant treatment options. Patients could take advantage of the use of the nomogram during the informed consent discussion regarding their prognosis, as it could offer a better assessment and understanding of the risks associated with this radiation therapy procedure.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

The development of the nomogram is in line with modern oncology trends which are looking to an individually tailored interdisciplinary patient treatment strategy capable going beyond the issue of organ preservation and focussing on the improvement of survival and the best possible quality of life. Modern interventional radiotherapy integrated in an interdisciplinary treatment schedule can therefore not only preserve the anatomical integrity of the eye, avoiding surgical enucleation, but also ensure better visual function.

COMPANY AWARD

GEC-ESTRO BEST JUNIOR PRESENTATION

Sponsored by Elekta Brachytherapy

IBTR: second conservative radio-surgical treatment with interstitial BT HDR. From 2D to 3D planning

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Department of Oncology-University of Torino - Italy

OVERVIEW OF THE ABSTRACT

The purpose of our study was to evaluate lumpectomy followed by interstitial BT HDR as a suitable salvage therapy for second tumour or recurrence of breast cancer after conservative surgery and post-operative EBRT.

The APBI (Accelerated Partial Breast Irradiation) rationale originates from pathologic data and patterns of failure showing that the residual disease and recurrences are largely confined to the tissues surrounding the lumpectomy cavity for patients with early stage breast cancer.

WHAT WERE THE THREE MAIN FINDINGS OF YOUR RESEARCH?

Patients selected had histologically confirmed IBTR and irrespective of histopathology, radical surgery with clear margins (≥2 mm) in all directions, ECOG PS: 0.

Local control was 87%, in the 2D group, and 95% in the 3D group, with three local relapses (respectively, 2 and 1). Global DFS was 94%. Cosmetic results defined by the NSABP cosmesis scale were satisfactory for the first 13 patients and excellent for the last 18 patients.

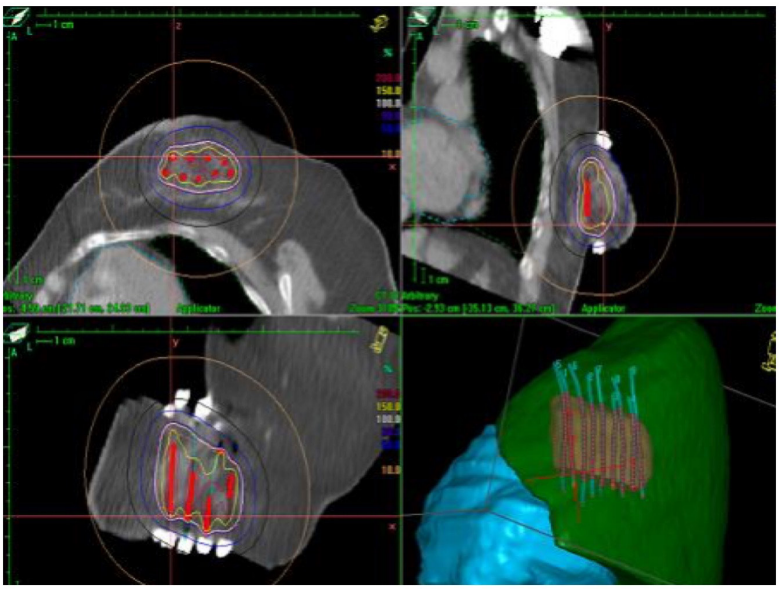
Selected patients with IBTR might benefit from less radical surgery in terms of body-image preservation and obtaining acceptable results such as local and distant control of the disease.

WHAT IMPACT COULD YOUR RESEARCH HAVE?

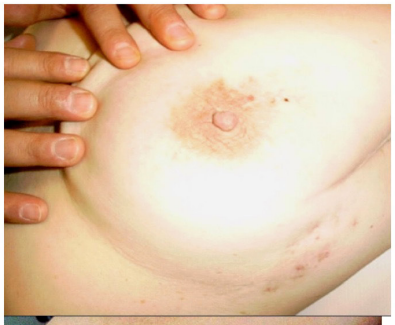
Partial breast irradiation after second BCS with MCB may be an alternative treatment strategy for patients who refuse mastectomy, despite being informed that this isconsidered the treatment of choice. Nowadays there is no evidence in the literature that salvage mastectomy with locoregional control rates of 90% results in significantly better control rates compared to a second conservative approach.

IS THIS RESEARCH INDICATIVE OF A BIGGER TREND IN ONCOLOGY?

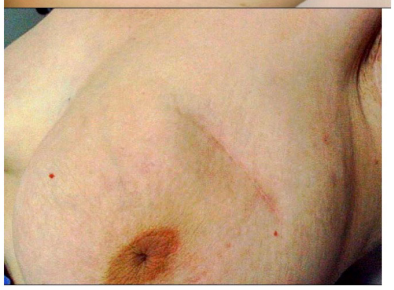
Our retrospective study shows that a second lumpectomy followed by HDR interstitial brachytherapy is a feasible treatment for IBTR and may be an alternative to salvage mastectomy. It offers very low complication rates and good cosmesis. Longer follow up and larger patient numbers are necessary to better define the role of salvage HDR brachytherapy. We believe that with careful selection criteria, there may be opportunities to individualize treatment options and to offer women a second chance at breast conservation.



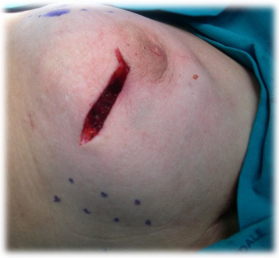
CT based 3D planning



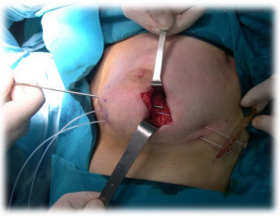
telangiectasia ⇒
dwell position too
close to skin surface



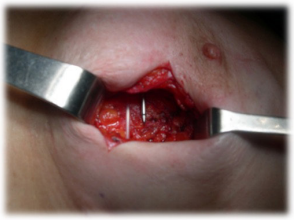
Good cosmetic results



Conserving surgery with lumpectomy cavity evaluation: a larger gap from the target cavity to the needles insertion point to avoid overdosing the skin



The steel needles are replaced with a plastic wires



Insertion of steel needles in a correct geometry

THANK YOU TO...

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