



ESTRO

NEWSLETTER MARCH - APRIL

ESTRO | EUROPEAN SOCIETY FOR RADIOTHERAPY & ONCOLOGY



BRACHYTHERAPY

Report on 6th GEC-
ESTRO workshop



PHYSICS

POP-ART RT survey.
Physicists get involved!



SCHOOL

Grants available to
Attend AMEE 2019
conference



CONFERENCE

ESTRO 38: what is in
store for you?

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NEWSLETTER N° 123
MARCH - APRIL 2019

Detail of the cathedrale Duomo di Milano, where ESTRO 38 will take place, 26-30 April 2019

ESTRO | EUROPEAN SOCIETY FOR RADIOTHERAPY & ONCOLOGY



EDITORIAL

“We will unveil ESTRO’s new strategy during the Presidential symposium on Sunday 28 April 2019”

Dear ESTRO colleagues,

With the Society’s annual meeting, ESTRO 38, just around the corner, I am really looking forward to meeting many of you again in Milan, Italy. The theme of this year’s meeting is ‘Targeting optimal care, together’. The scientific and organising committees have focused on these few, impactful words to put together a varied programme that shines the spotlight on the multi-professional and multidisciplinary aspects of our specialty. The theme also represents our strength: we are all working towards a common goal for improved patient outcomes, and this will be expressed throughout the scientific programme.

Judging by the impressive number of abstracts accepted – more than 2,000 – ESTRO 38 is the event most radiation oncology professionals will attend this year. The scientific quality of this year’s meeting will be enhanced further by the presence of more than ten randomised clinical trials, whose results will be presented in two dedicated sessions, including the ‘Late breaking abstracts’ session. ▼



Umberto Ricardi

We will unveil ESTRO's new strategy during the Presidential symposium on Sunday 28 April 2019. It will lead the way to achieving the ESTRO 2030 Vision: 'Radiation oncology. Optimal health for all, together', with a new vision statement built around four concepts of central importance to ESTRO.

As you arrive at ESTRO 38, you will also be greeted by the Society's new branding.

Finally, a last-minute reminder to our eligible ESTRO members that voting for four new Board members opened on 25 February and closes on 17 March 2019. If you have not done so yet, you still have some time to cast your vote. The new Board members will start their term at the general assembly on 29 April at ESTRO 38 in Milan.

See you all in Milan!

Warm regards,

Umberto Ricardi
ESTRO President



ESTRO 38 Deadlines

**Late registration:
26 March 2019**

**Desk registration:
from 27 March 2019**

BOARD MEMBERS ELECTIONS

In progress and ends 17 March 2019!



All ESTRO full members in 2019, who were also members in 2018, are eligible to vote for the four ESTRO Board directorship positions. This year, we are electing two clinicians, one physicist and one radiobiologist. ESTRO Board members are elected for a three-year term, which is renewable once. Candidates elected now will serve office until 2022.

By now all ESTRO members eligible to vote should have received a username and password with a link to the election platform. The official announcement of the new Board members and the beginning of their term will take place at the General Assembly during ESTRO 38 in Milan, Italy.

RADIOBIOLOGISTS



KAI ROTHKAMM



MARC VOOIJS

CLINICIANS



LENA SPECHT



ANNA KIRBY



MATTHIAS
GUCKENBERGER

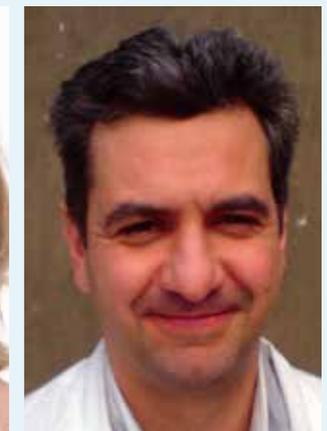


ALBERTO BOSSI

PHYSICISTS



NURIA JORNET



CLAUDIO FIORINO



READ IT BEFORE YOUR PATIENTS



READ IT BEFORE
YOUR PATIENTS

Too important to miss...

A digest of essential reading for all radiation oncologists

BY PHILIPPE LAMBIN, DIRK DE RUYSSCHER AND HANS KAANDERS



PHILIPPE LAMBIN



DIRK DE RUYSSCHER



HANS KAANDERS

INTRODUCTION

BREAST

PROSTATE

OROPHARYNGEAL

INTRACRANIAL

RECTAL

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TRIALS

RADIOSENSITIVITY



READ IT BEFORE
YOUR PATIENTS

BREAST

Long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: meta-analysis of individual patient data from ten randomised trials

Early Breast Cancer Trialists' Collaborative Group (EBCTCG), Asselain B, Barlow W, Bartlett J, Bergh J, Bergsten-Nordström E, Bliss J, Boccardo F, Boddington C, Bogaerts J, Bonadonna G, Bradley R, Brain E, Braybrooke J, Broet P, Bryant J, Burrett J, Cameron D, Clarke M, Coates A and 31 others

Lancet Oncol. 2018 Jan;19(1):27-39. doi: 10.1016/S1470-2045(17)30777-5. Epub 2017 Dec 11. Review

Background

Neoadjuvant chemotherapy (NACT) for early breast cancer can make breast-conserving surgery more feasible and might be more likely to eradicate micrometastatic disease than might the same chemotherapy given after surgery. We investigated the long-term benefits and risks of NACT and the influence of tumour characteristics on outcome with a collaborative meta-analysis of individual patient data from relevant randomised trials.

Methods

We obtained information about pre-randomisation tumour characteristics, clinical tumour response, surgery, recurrence, and mortality for 4,756 women in ten randomised trials in early breast cancer that began before 2005 and compared NACT with the same chemotherapy given postoperatively. Primary outcomes were tumour response, extent of local therapy, local and distant recurrence, breast cancer death, and overall mortality. Analyses by intention-to-treat used standard regression (for response and frequency of breast-conserving therapy) and log-rank methods (for recurrence and mortality).

Findings

Patients entered the trials from 1983 to 2002 and median follow-up was nine years (IQR 5–14), with the last follow-up in 2013. Most

chemotherapy was anthracycline based (3,838 [81%] of 4,756 women). More than two thirds (1,349 [69%] of 1947) of women allocated NACT had a complete or partial clinical response. Patients allocated NACT had an increased frequency of breast-conserving therapy (1,504 [65%] of 2,320 treated with NACT versus 1,135 [49%] of 2,318 treated with adjuvant chemotherapy). NACT was associated with more frequent local recurrence than was adjuvant chemotherapy: the 15-year local recurrence was 21.4% for NACT versus 15.9% for adjuvant chemotherapy (5.5% increase [95% CI 2.4–8.6]; rate ratio 1.37 [95% CI 1.17–1.61]; $p=0.0001$). No significant difference between NACT and adjuvant chemotherapy was noted for distant recurrence (15-year risk 38.2% for NACT versus 38.0% for adjuvant chemotherapy; rate ratio 1.02 [95% CI 0.92–1.14]; $p=0.66$), breast cancer mortality (34.4% vs 33.7%; 1.06 [0.95–1.18]; $p=0.31$), or death from any cause (40.9% vs 41.2%; 1.04 [0.94–1.15]; $p=0.45$).

Interpretation

Tumours downsized by NACT might have higher local recurrence after breast-conserving therapy than might tumours of the same dimensions in women who have not received NACT. Strategies to mitigate the increased local recurrence after breast-conserving therapy in tumours downsized by NACT should be considered – e.g. careful tumour localisation, detailed pathological assessment and appropriate radiotherapy.



READ IT BEFORE
YOUR PATIENTS

BREAST

Patient-reported outcomes over five years after whole- or partial-breast radiotherapy: longitudinal analysis of the IMPORT LOW (CRUK/06/003) phase III randomised controlled trial

Bhattacharya IS, Haviland JS, Kirby AM, Kirwan CC, Hopwood P, Yarnold JR, Bliss JM, Coles CE; IMPORT Trialists.

J Clin Oncol. 2018 Dec 11, doi: 10.1200/JCO.18.00982. [Epub ahead of print]

Purpose

IMPORT LOW demonstrated non-inferiority of partial-breast and reduced-dose radiotherapy versus whole-breast radiotherapy for local relapse and similar or reduced toxicity at five years. Comprehensive patient-reported outcome measures collected at serial time points are now reported.

Patients and methods

IMPORT LOW recruited women with low-risk breast cancer after breast-conserving surgery. Patients were randomly assigned to 40 Gy whole-breast radiotherapy (control), 36 Gy whole-breast and 40 Gy partial-breast radiotherapy (reduced-dose), or 40 Gy partial-breast radiotherapy only (partial-breast) in 15 fractions. European Organisation for Research and Treatment of Cancer Quality of Life Questionnaires Core 30 and Breast Cancer-Specific Module, Body Image Scale, protocol-specific items, and the Hospital Anxiety and Depression Scale were administered at baseline, six months, and one, two, and five years. Patterns of moderate/marked adverse effects (AEs) were assessed using longitudinal regression models, and baseline predictors were investigated.

Results

A total of 41 of 71 centres participated in the patient-reported outcome measures sub-study;

1,265 (95%) of 1,333 patients consented, and 557 (58%) of 962 reported no moderate/marked AEs at five years. Breast appearance change was most prevalent and persisted over time (approximately 20% at each time point). Prevalence of breast hardness, pain, oversensitivity, oedema, and skin changes reduced over time ($P < .001$ for each), whereas breast shrinkage increased ($P < .001$). Analysis by treatment group showed average number of AEs per person was lower in partial-breast (incidence rate ratio, 0.77; 95% CI, 0.71 to 0.84; $P < .001$) and reduced-dose (incidence rate ratio, 0.83; 95% CI, 0.76 to 0.90; $P < .001$) versus whole-breast group and decreased over time in all groups. Younger age, larger breast size/surgical deficit, lymph node positivity, and higher levels of anxiety/depression were baseline predictors of subsequent AE reporting.

Conclusion

Most AEs reduced over time, with fewer AEs in the partial-breast and reduced-dose groups. Baseline predictors for AE reporting were identified. These findings will facilitate informed discussion and shared decision-making for future patients receiving moderately hypofractionated breast radiotherapy.



READ IT BEFORE
YOUR PATIENTS

BREAST

Association of CD4+ radiation-induced lymphocyte apoptosis with fibrosis and telangiectasia after radiotherapy in 272 breast cancer patients with >10-year follow-up

Veldwijk MR, Seibold P, Botma A, Helmbold I, Sperk E, Giordano FA, Gürth N, Kirchner A, Behrens S, Wenz F, Chang-Claude J, Herskind C.

Clin Cancer Res. 2018, doi: 10.1158/1078-0432.CCR-18-0777 [Epub ahead of print]

Purpose

Radiation-induced lymphocyte apoptosis (RILA) has been suggested as a predictive assay for adverse late reactions after radiotherapy. Thus, low RILA values of T-lymphocyte sub-populations have been associated with increased risk for various endpoints at two to three years of follow-up. The purpose was to test if such associations persist for specific endpoints (subcutaneous fibrosis, telangiectasia) in breast cancer patients with at least ten years of follow-up.

Experimental design

Two hundred and seventy-two female patients who had received breast-conserving therapy within the German ISE study were included (median follow-up: 11.6 years). Radiotherapy-induced side effects were scored according to the Late Effects in Normal Tissues-Subjective, Objective, Management, and Analytic (LENT-SOMA) classification system. RILA in the CD4+, CD8+, and natural killer (NK) sub-populations from peripheral blood was analysed by flow cytometry. Multivariate predictive modelling was performed, including relevant clinical risk factors.

Results

Low CD4+ RILA was associated with increased risk for both fibrosis (P = 0.011) and telangiectasia

(P < 0.001). For fibrosis, the association was stronger outside the surgical area (Fibout; P = 0.004) than within (Fibin; P = 0.17). Predictive multivariate modelling, including clinical risk factors yielded OR of 3.48 (95% confidence interval, 1.84-6.58) for any fibrosis and 8.60 (2.71-27.3) for telangiectasia. Addition of CD4+ RILA to the clinical variables improved discrimination (c statistics) from 0.62 to 0.68 for any fibrosis, 0.62 to 0.66 for Fibin, 0.61 to 0.69 for Fibout, and from 0.65 to 0.76 for telangiectasia. CD8+ and NK RILA were not significantly associated with radiotherapy-related late reactions.

Conclusions

The results provide the first evidence that low CD4+ RILA is associated with increased subcutaneous fibrosis and telangiectasia even after ten years. This supports the potential usefulness for predicting individual clinical risk.



READ IT BEFORE
YOUR PATIENTS

PROSTATE

Short-term androgen suppression and radiotherapy versus intermediate-term androgen suppression and radiotherapy, with or without zoledronic acid, in men with locally advanced prostate cancer (TROG 03.04 RADAR): ten-year results from a randomised, phase 3, factorial trial

Denham JW, Joseph D, Lamb DS, Spry NA, Duchesne G, Matthews J, Atkinson C, Tai KH, Christie D, Kenny L, Turner S, Gogna NK, Diamond T, Delahunt B, Oldmeadow C, Attia J, Steigler A

Lancet: December 19, 2018, doi :[https://doi.org/10.1016/S1470-2045\(18\)30757-5](https://doi.org/10.1016/S1470-2045(18)30757-5)

Background

The optimal duration of androgen suppression for men with locally advanced prostate cancer receiving radiotherapy with curative intent is yet to be defined. Zoledronic acid is effective in preventing androgen suppression-induced bone loss, but its role in preventing castration-sensitive bone metastases in locally advanced prostate cancer is unclear. The RADAR trial assessed whether the addition of 12 months of adjuvant androgen suppression, 18 months of zoledronic acid, or both, can improve outcomes in men with locally advanced prostate cancer who receive six months of androgen suppression and prostatic radiotherapy. This report presents ten-year outcomes from this trial.

Methods

For this randomised, phase 3, 2 × 2 factorial trial, eligible men were 18 years or older with locally advanced prostate cancer (either T2b-4, N0 M0 tumours or T2a, N0 M0 tumours provided Gleason score was ≥7 and baseline prostate-specific antigen [PSA] concentration was ≥10 µg/L). We randomly allocated participants in a 2 × 2 factorial design by computer-generated randomisation (using the minimisation technique, and stratified by centre, baseline PSA concentration, clinical tumour stage, Gleason score, and use of a brachytherapy boost) in a 1:1:1:1 ratio to four treatment groups. Patients in the control group

received six months of neoadjuvant androgen suppression with leuprorelin (22.5 mg every three months, intramuscularly) and radiotherapy alone (short-term androgen suppression [STAS]); this treatment was either followed by another 12 months of adjuvant androgen suppression with leuprorelin (22.5 mg every three months, intramuscularly; intermediate-term androgen suppression [ITAS]), or accompanied by 18 months of zoledronic acid (4 mg every three months, intravenously) starting at randomisation (STAS plus zoledronic acid), or both (ITAS plus zoledronic acid). All patients received radiotherapy to the prostate and seminal vesicles, starting from the end of the fifth month of androgen suppression; dosing options were 66, 70, and 74 Gy in 2-Gy fractions per day, or 46 Gy in 2-Gy fractions followed by a high-dose-rate brachytherapy boost dose of 19.5 Gy in 6.5-Gy fractions. Treatment allocation was open label. The primary endpoint was prostate cancer-specific mortality and was analysed according to intention-to-treat using competing-risks methods. The trial is closed to follow-up and this is the final report of the main endpoints. This trial is registered with ClinicalTrials.gov, number NCT00193856.

Findings

Between 20 October 2003 and 15 August 2007, 1,071 men were enrolled and randomly assigned to STAS (n=268), ITAS (n=268), STAS plus zoledronic acid (n=268), and ITAS plus ▼

zoledronic acid (n=267). Median follow-up was 10.4 years (IQR 7.9–11.7). At this ten-year follow-up, no interactions were observed between androgen suppression and zoledronic acid, so the treatment groups were collapsed to compare treatments according to duration of androgen suppression: six months of androgen suppression plus radiotherapy (6AS+RT) versus 18 months of androgen suppression plus radiotherapy (18AS+RT) and to compare treatments according to whether or not patients received zoledronic acid. The total number of deaths was 375 (200 men receiving 6AS+RT and 175 men receiving 18AS+RT), of which 143 (38%) were attributable to prostate cancer (81 men receiving 6AS+RT and 62 men receiving 18AS+RT). When analysed by duration of androgen suppression, the adjusted cumulative incidence of prostate cancer-specific mortality was 13.3% (95% CI 10.3–16.0) for 6AS+RT versus 9.7% (7.3–12.0) for 18AS+RT, representing an absolute difference of 3.7% (95% CI 0.3–7.1; sub-hazard ratio [sHR] 0.70 [95% CI 0.50–0.98], adjusted p=0.035). The addition of zoledronic acid did not affect prostate cancer-specific mortality; the adjusted cumulative incidence of prostate cancer-specific mortality was 11.2% (95% CI 8.7–13.7) with zoledronic acid versus 11.7% (9.2–14.1) without, representing an absolute difference of –0.5% (95% CI –3.8 to 2.9; sHR 0.95 [95% CI 0.69–1.32], adjusted p=0.78). Although safety analysis was not pre-specified for this ten-year analysis, one new serious adverse event (osteonecrosis of the mandible, in a patient who received 18 months of androgen suppression

plus zoledronic acid) occurred since our previous report, bringing the total number of cases of this serious adverse event to three (<1% out of 530 patients who received zoledronic acid evaluated for safety) and the total number of drug-related serious adverse events to 12 (1% out of all 1,065 patients evaluable for safety). No treatment-related deaths occurred during the study.

Interpretation

This study shows that 18 months of androgen suppression plus radiotherapy is a more effective treatment option for locally advanced prostate cancer than six months of androgen suppression plus radiotherapy, but the addition of zoledronic acid to this treatment regimen is not beneficial. Evidence from the RADAR and French Canadian Prostate Cancer Study IV trials suggests that 18 months of androgen suppression with moderate radiation dose escalation is an effective but more tolerable option than longer durations of androgen suppression for men with locally advanced prostate cancer, including intermediate and high risk elements.



READ IT BEFORE
YOUR PATIENTS

PROSTATE

Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial

Parker CC, James ND, Brawley CD, Clarke NW, Hoyle AP, Ali A, Ritchie AWS, Attard G, Chowdhury S, Cross W, Dearnaley DP, Gillissen S, Gilson C, Jones RJ, Langlely RE, Malik ZI, Mason MD, Matheson D, Millman R, Russell JM, Thalmann GN, Amos CL, Alonzi R, Bahl A, Birtle A, Din O, Douis H, Eswar C, Gale J, Gannon MR, Jonnada S, Khaksar S, Lester JF, O'Sullivan JM, Parikh OA, Pedley ID, Pudney DM, Sheehan DJ, Srihari NN, Tran ATH, Parmar MKB, Sydes MR; Systemic Therapy for Advanced or Metastatic Prostate cancer: Evaluation of Drug Efficacy (STAMPEDE) investigators.

Lancet. 2018 Dec 1;392(10162):2353-2366. doi: 10.1016/S0140-6736(18)32486-3

Background

Based on previous findings, the study group hypothesised that radiotherapy to the prostate would improve overall survival in men with metastatic prostate cancer, and that the benefit would be greatest in patients with a low metastatic burden. We aimed to compare standard of care for metastatic prostate cancer, with and without radiotherapy.

Methods

The group did a randomised controlled phase 3 trial at 117 hospitals in Switzerland and the UK. Eligible patients had newly diagnosed metastatic prostate cancer. We randomly allocated patients open-label in a 1:1 ratio to standard of care (control group) or standard of care and radiotherapy (radiotherapy group). Randomisation was stratified by hospital, age at randomisation, nodal involvement, World Health Organization (WHO) performance status, planned androgen deprivation therapy, planned docetaxel use (from December 2015), and regular aspirin or non-steroidal anti-inflammatory drug use. Standard of care was lifelong androgen deprivation therapy, with up-front docetaxel permitted from December 2015. Men allocated radiotherapy received either a daily (55 Gy in 20 fractions over four weeks) or weekly (36 Gy in six fractions over six weeks) schedule that was nominated before randomisation. The metastatic burden was classified according to

the definition used in the CHAARTED trial: high metastatic burden was defined as four or more bone metastases with one or more outside the vertebral bodies or pelvis, or visceral metastases, or both; all other assessable patients were considered to have low metastatic burden. The primary outcome was overall survival, measured as the number of deaths; this analysis had 90% power with a one-sided α of 2.5% for a hazard ratio (HR) of 0.75. Secondary outcomes were failure-free survival, progression-free survival, metastatic progression-free survival, prostate cancer-specific survival, and symptomatic local event-free survival. Two pre-specified subgroup analyses tested the effects of prostate radiotherapy by baseline metastatic burden and radiotherapy schedule.

Findings

Between 22 January 2013 and 2 September 2016, 2,061 men underwent randomisation, 1,029 were allocated the control and 1032 radiotherapy. Allocated groups were balanced, with a median age of 68 years (IQR 63-73) and median amount of prostate-specific antigen of 97 ng/mL (33-315). In total, 367 (18%) patients received early docetaxel; 1,082 (52%) participants nominated the daily radiotherapy schedule before randomisation, and 979 (48%) the weekly schedule; 819 (40%) men had a low metastatic burden, 1,120 (54%) had a high metastatic burden, and the metastatic burden was unknown for 122 (6%). ▼

A total of 643 (84%) of 761 deaths were attributed to prostate cancer (329 [84%] of 391 in the control group and 314 [85%] of 370 in the radiotherapy group). Adjusted competing risks regression for prostate cancer-specific survival using the Fine and Gray method provided no evidence of an overall treatment effect (sub-HR 0.94, 95% CI 0.81–1.10; robust $p=0.431$). There was evidence of an effect in patients with low metastatic burden (sub-HR 0.65, 95% CI 0.47–0.90; robust $p=0.010$), but no evidence of a treatment effect was noted in patients with high metastatic burden (1.11, 0.92–1.33; robust $p=0.279$). A significant interaction was seen between treatment effect and metastatic burden (robustly estimated interaction $p=0.007$).

In the pre-specified subgroup analysis by metastatic burden, failure-free survival was improved in patients with low metastatic burden at baseline who were allocated radiotherapy (HR 0.59, 95% CI 0.49–0.72; $p<0.0001$). Evidence of a differential treatment effect from radiotherapy compared with the high metastatic burden subgroup was also noted (interaction $p=0.002$; HR 0.88, 95% CI 0.77–1.01; $p=0.059$).

Radiotherapy was well tolerated, with 48 (5%) adverse events (Radiation Therapy Oncology Group grade 3-4) reported during radiotherapy and 37 (4%) after radiotherapy. The proportion reporting at least one severe adverse event (Common Terminology Criteria for Adverse Events grade 3 or worse) was similar by treatment

group in the safety population (398 [38%] with control and 380 [39%] with radiotherapy).

Interpretation

This randomised comparison of more than 2,000 patients with metastatic prostate cancer showed that local radiotherapy to the prostate did not improve overall survival for unselected patients. However, a pre-specified analysis showed that prostate radiotherapy did improve overall survival (from 73% to 81% at three years) in those with a low metastatic burden, which represented 40% of the comparison population.



READ IT BEFORE
YOUR PATIENTS

OROPHARYNGEAL

Radiotherapy plus cetuximab or cisplatin in human papillomavirus-positive oropharyngeal cancer (NRG Oncology RTOG 1016): a randomised, multicentre, non-inferiority trial

Gillison ML, Trotti AM, Harris J, Eisbruch A, Harari PM, Adelstein DJ, Sturgis EM, Burtness B, Ridge JA, Ringash J, Galvin J, Yao M, Koyfman SA, Blakaj DM, Razaq MA, Colevas AD, Beitler JJ, Jones CU, Dunlap NE, Seaward SA, Spencer S, Galloway TJ, Phan J, Dignam JJ, Le QT.

Lancet. 2018 Nov 15. pii: S0140-6736(18)32779-X. doi: 10.1016/S0140-6736(18)32779-X. [Epub ahead of print]

Background

Patients with human papillomavirus (HPV)-positive oropharyngeal squamous cell carcinoma have high survival rates when treated with radiotherapy plus cisplatin. However, it is not known whether replacement of cisplatin with cetuximab – an antibody against the epidermal growth factor receptor – can preserve these high survival rates and reduce treatment toxicity. We investigated whether cetuximab would maintain a high proportion of patient survival and reduce acute and late toxicity.

Methods

RTOG 1016 was a randomised, multicentre, non-inferiority trial at 182 healthcare centres in the USA and Canada. Eligibility criteria included histologically confirmed HPV-positive oropharyngeal carcinoma; American Joint Committee on Cancer 7th edition clinical categories T1-T2, N2a-N3 M0 or T3-T4, N0-N3 M0; Zubrod performance status 0 or 1; age at least 18 years; and adequate bone marrow, hepatic, and renal function. We randomly assigned patients (1:1) to receive either radiotherapy plus cetuximab or radiotherapy plus cisplatin. Randomisation was balanced by using randomly permuted blocks, and patients were stratified by T category (T1-T2 vs T3-T4), N category (N0-N2a vs N2b-N3), Zubrod performance status (0 vs 1), and tobacco smoking history (≤ 10 pack-years vs >10 pack-years). Patients were assigned

to receive either intravenous cetuximab at a loading dose of 400 mg/m² five to seven days before radiotherapy initiation, followed by cetuximab 250 mg/m² weekly for seven doses (total 2150 mg/m²), or cisplatin 100 mg/m² on days 1 and 22 of radiotherapy (total 200 mg/m²). All patients received accelerated intensity-modulated radiotherapy delivered at 70 Gy in 35 fractions over six weeks at six fractions per week (with two fractions given on one day, at least six hours apart). The primary endpoint was overall survival, defined as time from randomisation to death from any cause, with non-inferiority margin 1.45. Primary analysis was based on the modified intention-to-treat approach, whereby all patients meeting eligibility criteria are included. This study is registered with ClinicalTrials.gov, number NCT01302834.

Findings

Between 9 June 2011 and 31 July 2014, 987 patients were enrolled, of whom 849 were randomly assigned to receive radiotherapy plus cetuximab (n=425) or radiotherapy plus cisplatin (n=424). In total, 399 patients who were assigned to receive cetuximab and 406 patients assigned to receive cisplatin were subsequently eligible. After median follow-up duration of 4.5 years, radiotherapy plus cetuximab did not meet the non-inferiority criteria for overall survival (hazard ratio [HR] 1.45, one-sided 95% upper CI 1.94; p=0.5056 for non-inferiority; one-sided log-rank p=0.0163). Estimated five-year overall ▼

survival was 77.9% (95% CI 73.4-82.5) in the cetuximab group versus 84.6% (80.6-88.6) in the cisplatin group. Progression-free survival was significantly lower in the cetuximab group compared with the cisplatin group (HR 1.72, 95% CI 1.29-2.29; $p=0.0002$; five-year progression-free survival 67.3%, 95% CI 62.4-72.2 vs 78.4%, 73.8-83.0), and locoregional failure was significantly higher in the cetuximab group compared with the cisplatin group (HR 2.05, 95% CI 1.35-3.10; five-year proportions 17.3%, 95% CI 13.7-21.4 vs 9.9%, 6.9-13.6). Proportions of acute moderate to severe toxicity (77.4%, 95% CI 73.0-81.5 vs 81.7%, 77.5-85.3; $p=0.1586$) and late moderate to severe toxicity (16.5%, 95% CI 12.9-20.7 vs 20.4%, 16.4-24.8; $p=0.1904$) were similar between the cetuximab and cisplatin groups.

Interpretation

For patients with HPV-positive oropharyngeal carcinoma, radiotherapy plus cetuximab showed inferior overall survival and progression-free survival compared with radiotherapy plus cisplatin. Radiotherapy plus cisplatin is the standard of care for eligible patients with HPV-positive oropharyngeal carcinoma.



READ IT BEFORE
YOUR PATIENTS

OROPHARYNGEAL

Radiotherapy plus cisplatin or cetuximab in low-risk human papillomavirus-positive oropharyngeal cancer (De-ESCALaTE HPV): an open-label randomised controlled phase 3 trial

Mehanna H, Robinson M, Hartley A, Kong A, Foran B, Fulton-Lieuw T, Dalby M, Mistry P, Sen M, O'Toole L, Al Booz H, Dyker K, Moleron R, Whitaker S, Brennan S, Cook A, Griffin M, Aynsley E, Rolles M, De Winton E, Chan A, Srinivasan D, Nixon I, Grumett J, Leemans CR, Buter J, Henderson J, Harrington K, McConkey C, Gray A, Dunn J; De-ESCALaTE HPV Trial Group.

Lancet. 2018 Nov 15. pii: S0140-6736(18)32752-1. doi: 10.1016/S0140-6736(18)32752-1. [Epub ahead of print]

Background

The incidence of human papillomavirus (HPV)-positive oropharyngeal cancer, a disease affecting younger patients, is rapidly increasing. Cetuximab, an epidermal growth factor receptor inhibitor, has been proposed for treatment de-escalation in this setting to reduce the toxicity of standard cisplatin treatment, but no randomised evidence exists for the efficacy of this strategy.

Methods

We did an open-label randomised controlled phase 3 trial at 32 head and neck treatment centres in Ireland, The Netherlands, and the UK, in patients aged 18 years or older with HPV-positive low-risk oropharyngeal cancer (non-smokers or lifetime smokers with a smoking history of <10 pack-years). Eligible patients were randomly assigned (1:1) to receive, in addition to radiotherapy (70 Gy in 35 fractions), either intravenous cisplatin (100 mg/m² on days 1, 22, and 43 of radiotherapy) or intravenous cetuximab (400 mg/m² loading dose followed by seven weekly infusions of 250 mg/m²). The primary outcome was overall severe (grade 3-5) toxicity events at 24 months from the end of treatment. The primary outcome was assessed by intention-to-treat and per-protocol analyses. This trial is registered with the ISRCTN registry, number ISRCTN33522080.

Findings

Between 12 November 2012 and 1 October 2016, 334 patients were recruited (166 in the cisplatin group and 168 in the cetuximab group). Overall (acute and late) severe (grade 3-5) toxicity did not differ significantly between treatment groups at 24 months (mean number of events per patient 4.8 [95% CI 4.2-5.4] with cisplatin versus 4.8 [4.2-5.4] with cetuximab; $p=0.98$). At 24 months, overall all-grade toxicity did not differ significantly either (mean number of events per patient 29.2 [95% CI 27.3-31.0] with cisplatin versus 30.1 [28.3-31.9] with cetuximab; $p=0.49$). However, there was a significant difference between cisplatin and cetuximab in two-year overall survival (97.5% vs 89.4%, hazard ratio 5.0 [95% CI 1.7-14.7]; $p=0.001$) and two-year recurrence (6.0% vs 16.1%, 3.4 [1.6-7.2]; $p=0.0007$).

Interpretation

Compared with the standard cisplatin regimen, cetuximab showed no benefit in terms of reduced toxicity, but instead showed significant detriment in terms of tumour control. Cisplatin and radiotherapy should be used as the standard of care for HPV-positive low-risk patients who are able to tolerate cisplatin.



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READ IT BEFORE
YOUR PATIENTS

INTRACRANIAL

Risk of radiation-associated intracranial malignancy after stereotactic radiosurgery: a retrospective, multicentre, cohort study

Wolf A, Naylor K, Tam M, Habibi A, Novotny J, Liščák R, Martinez-Moreno N, Martinez-Alvarez R, Sisterson N, Golfinos JG, Silverman J, Kano H, Sheehan J, Lunsford LD, Kondziolka D.

Lancet Oncol. 2018 Nov 22. pii: S1470-2045(18)30659-4. doi: 10.1016/S1470-2045(18)30659-4. [Epub ahead of print]

Background

A major concern of patients who have stereotactic radiosurgery is the long-term risk of having a secondary intracranial malignancy or, in the case of patients with benign tumours treated with the technique, the risk of malignant transformation. The incidence of stereotactic radiosurgery-associated intracranial malignancy remains unknown; therefore, our aim was to estimate it in a population-based study to assess the long-term safety of this technique.

Methods

We did a population-based, multicentre, cohort study at five international radiosurgery centres (Na Homolce Hospital, Prague, Czech Republic [n=2655 patients]; Ruber International Hospital, Madrid, Spain [n=1080], University of Pittsburgh Medical Center, Pittsburgh, PA, USA [n=1027]; University of Virginia, Charlottesville, VA, USA [n=80]; and NYU Langone Health System, New York, NY, USA [n=63]). Eligible patients were of any age, and had Gamma Knife radiosurgery for arteriovenous malformation, trigeminal neuralgia, or benign intracranial tumours, which included vestibular or other benign schwannomas, WHO grade 1 meningiomas, pituitary adenomas, and haemangioblastoma. Patients were excluded if they had previously had radiotherapy or did not have a minimum follow-up time of five years. The primary objective of the study was to estimate the incidence of stereotactic

radiosurgery-associated intracranial malignancy, including malignant transformation of a benign lesion or development of radiation-associated secondary intracranial cancer, defined as within the 2 Gy isodose line. Estimates of age-adjusted incidence of primary CNS malignancies in the USA and European countries were retrieved from the Central Brain Tumour Registry of the United States (CBTRUS) and the International Agency for Research on Cancer (IARC) Global Cancer statistics.

Findings

Of 14,168 patients who had Gamma Knife stereotactic radiosurgery between 14 August 1987 and 31 December 2011, in the five contributing centres, 4,905 patients were eligible for the analysis (had a minimum follow-up of five years and no history of previous radiation therapy). Diagnostic entities included vestibular schwannomas (1,011 [20.6%] of 4,905 patients), meningiomas (1,490 [30.4%]), arteriovenous malformations (1,089 [22.2%]), trigeminal neuralgia (565 [11.5%]), pituitary adenomas (641 [13.1%]), haemangioblastoma (29 [0.6%]), and other schwannomas (80 [1.6%]). With a median follow-up of 8.1 years (IQR 6.0–10.6), two (0.0006%) of 3,251 patients with benign tumours were diagnosed with suspected malignant transformation and one (0.0002%) of 4,905 patients was considered a case of radiosurgery-associated intracranial malignancy, resulting in an incidence of 6.87 per 100,000 patient-years ▼

(95% CI 1.15–22.71) for malignant transformation and 2.26 per 100,000 patient-years (0.11–11.17) for radiosurgery-associated intracranial malignancy. Two (0.0004%) of 4,905 patients developed intracranial malignancies, which were judged unrelated to the radiation field. Overall incidence of radiosurgery-associated malignancy was 6.80 per 100,000 patients-years (95% CI 1.73–18.50), or a cumulative incidence of 0.00045% over ten years (95% CI 0.00–0.0034). The overall incidence of 6.8 per 100,000, which includes institutions from Europe and the USA, after stereotactic radiosurgery was found to be similar to the risk of developing a malignant CNS tumour in the general population of the USA and some European countries as estimated by the CBTRUS and IARC data, respectively.

Interpretation

These data show that the estimated risk of an intracranial secondary malignancy or malignant transformation of a benign tumour in patients treated with stereotactic radiosurgery remains low at long-term follow-up, and is similar to the risk of the general population to have a primary CNS tumour. Although prospective cohort studies with longer follow-up are warranted to support the results of this study, the available evidence suggests the long-term safety of stereotactic radiosurgery and could support physicians counselling patients on Gamma Knife stereotactic radiosurgery.

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READ IT BEFORE
YOUR PATIENTS

RECTAL

Neoadjuvant (chemo)radiotherapy with total mesorectal excision only is not sufficient to prevent lateral local recurrence in enlarged nodes: results of the multi-centre lateral node study of patients with low ct3/4 rectal cancer

Ogura A, Konishi T, Cunningham C, Garcia-Aguilar J, Iversen H, Toda S, Lee IK, Lee HX, Uehara K, Lee P, Putter H, van de Velde CJH, Beets GL, Rutten HJT, Kusters M; Lateral Node Study Consortium.

J Clin Oncol. 2019 Jan 1;37(1):33-43. doi: 10.1200/JCO.18.00032. Epub 2018 Nov 7

Purpose

Improvements in magnetic resonance imaging (MRI), total mesorectal excision (TME) surgery, and the use of (chemo)radiotherapy [(C)RT] have improved local control of rectal cancer; however, we have been unable to eradicate local recurrence (LR). Even in the face of TME and negative resection margins (R0), a significant proportion of patients with enlarged lateral lymph nodes (LLNs) suffer from lateral LR (LLR). Japanese studies suggest that the addition of an LLN dissection (LLND) could reduce LLR. This multi-centre pooled analysis aims to ascertain whether LLNs actually pose a problem and whether LLND results in fewer LLRs.

Patients and methods

Data from 1,216 consecutive patients with cT3/T4 rectal cancers up to 8cm from the anal verge who underwent surgery in a five-year period were collected. LLND was performed in 142 patients (12%). MRIs were re-evaluated with a standardised protocol to assess LLN features.

Results

On pre-treatment MRI, 703 patients (58%) had visible LLN, and 192 (16%) had a short axis of at least 7 mm. One hundred and eight patients developed LR (five-year LR rate, 10.0%), of which 59 (54%) were LLRs (five-year LLR rate, 5.5%). After multivariable analyses, LLNs with a short

axis of at least 7 mm resulted in a significantly higher risk of LLR (hazard ratio, 2.060; $P = .045$) compared with LLNs of less than 7 mm. In patients with LLNs at least 7 mm, (C)RT plus TME plus LLND resulted in a five-year LLR of 5.7%, which was significantly lower than that in patients who underwent (C)RT plus TME (five-year LLR, 19.5%; $P = .042$).

Conclusion

LLR is still a significant problem after (C)RT plus TME in LLNs with a short axis at least 7 mm on pre-treatment MRI. The addition of LLND results in a significantly lower LLR rate.

COMMENT

Professor Karin Haustermans
*University Hospital Gasthuisberg,
Leuven, Belgium*

This paper by Ogura *et al* describes the results of a multicentre pooled analysis lateral node study in 1,216 patients with low cT3/T4 rectal cancer. The authors showed that lateral lymph nodes (LLN) with a short axis of at least 7 mm (which is a substantially enlarged lymph node) resulted in a significantly higher risk of lateral local recurrence (LLR) (hazard ratio 2.060; $p=0.045$), especially in those patients who did not undergo a lateral lymph node dissection at the time of total mesorectal excision (TME) surgery.

Only 16% of the patients ($n=192$) had LLN with a short axis of at least 7 mm. In total, 59 patients developed an LLR. The risk of an LLR was significantly lower in patients who underwent TME plus lateral lymph node dissection (LLND). Although these results are unique, they should be interpreted with caution. Although this is the largest dataset currently available, overall patient numbers in the study are still small. Patients were treated with or without short-course radiotherapy

or long-course chemoradiotherapy. The total dose of radiation, the fractionation, the volume irradiated and the drugs used are not mentioned. Not all patients underwent restaging MRI, the interval to surgery is not reported and a minority of patients received adjuvant chemotherapy. Moreover, LLND was only performed in a subgroup of hospitals. From table A2 it is also clear that guidelines on preoperative treatment in locally advanced rectal cancer differ substantially between countries, especially in Japan where not all patients with locally advanced rectal cancer were treated with preoperative radiotherapy.

What can we learn from this publication?

Locoregional staging by MRI interpreted by an experienced radiologist is a prerequisite in the treatment of this disease. All patients with a new diagnosis of rectal cancer should be discussed at a multidisciplinary team meeting. In patients where LLN are present with a short axis of 7 mm or more, a long course of chemoradiation should be offered with restaging MRI six to eight weeks after the end of the chemoradiation. If the LLN remain suspect on multiparametric MRI, a LLND should be considered. In this study LLN enlargement did not influence distant recurrence. This might indicate that intensifying the preoperative treatment by increasing the radiation dose is preferable to intensifying the

chemotherapy in cases where LLN are present at initial staging. As the authors rightly point out, these important questions can only be answered in a large prospective multicentre setting with high-volume referral centres for locally advanced rectal cancer, where expertise in radiotherapy and surgery can be standardised and quality controlled.



KARIN
HAUSTERMANS



READ IT BEFORE
YOUR PATIENTS

RECTAL

Long-term outcomes of clinical complete responders after neoadjuvant treatment for rectal cancer in the International Watch & Wait Database (IWWD): an international multicentre registry study

Maxime J M van der Valk, Denise E Hilling, Esther Bastiaannet, Elma Meershoek-Klein Kranenbarg, Geerard L Beets, Nuno L Figueiredo, Prof Angelita Habr-Gama, Rodrigo O Perez, Andrew G Renehan, Cornelis J H van de Velde, and the IWWD Consortium

Lancet, Vol 391, ISSUE 10139, P2537-2545, June 23, 2018, doi: [https://doi.org/10.1016/S0140-6736\(18\)31078-X](https://doi.org/10.1016/S0140-6736(18)31078-X)

Background

The strategy of watch and wait (W&W) in patients with rectal cancer who achieve a complete clinical response (cCR) after neoadjuvant therapy is new and offers an opportunity for patients to avoid major resection surgery. However, evidence is based on small-to-moderate sized series from specialist centres. The International Watch & Wait Database (IWWD) aims to describe the outcome of the W&W strategy in a large-scale registry of pooled individual patient data. We report the results of a descriptive analysis after inclusion of more than 1,000 patients in the registry.

Methods

Participating centres entered data in the registry through an online, highly secured, and encrypted research data server. Data included baseline characteristics, neoadjuvant therapy, imaging protocols, incidence of local regrowth and distant metastasis, and survival status. All patients with rectal cancer in whom the standard of care (total mesorectal excision surgery) was omitted after neoadjuvant therapy were eligible to be included in the IWWD. For the present analysis, we only selected patients with no signs of residual tumour at reassessment (a cCR). We analysed the proportion of patients with local regrowth, proportion of patients with distant metastases, five-year overall survival, and five-year disease-specific survival.

Findings

Between 14 April 2015 and 30 June 2017, we identified 1,009 patients who received neoadjuvant treatment and were managed by W&W in the database from 47 participating institutes (15 countries). We included 880 (87%) patients with a cCR. Median follow-up time was 3.3 years (95% CI 3.1–3.6). The two-year cumulative incidence of local regrowth was 25.2% (95% CI 22.2–28.5%), 88% of all local regrowth was diagnosed in the first two years, and 97% of local regrowth was located in the bowel wall. Distant metastas were diagnosed in 71 (8%) of 880 patients. Five-year overall survival was 85% (95% CI 80.9–87.7%), and five-year disease-specific survival was 94% (91–96%).

Interpretation

This dataset has the largest series of patients with rectal cancer treated with a W&W approach, consisting of approximately 50% data from previous cohort series and 50% unpublished data. Local regrowth occurs mostly in the first two years and in the bowel wall, emphasising the importance of endoscopic surveillance to ensure the option of deferred curative surgery. Local unsalvageable disease after W&W was rare.



READ IT BEFORE
YOUR PATIENTS

GLIOBLASTOMA

Regorafenib compared with lomustine in patients with relapsed glioblastoma (REGOMA): a multicentre, open-label, randomised, controlled, phase 2 trial

Lombardi G, De Salvo GL, Brandes AA, Eoli M, Rudà R, Faedi M, Lolli I, Pace A, Daniele B, Pasqualetti F, Rizzato S, Bellu L, Pambuku A, Farina M, Magni G, Indraccolo S, Gardiman MP, Soffietti R, Zagonel V

Lancet Oncol. 2018 Dec 3. pii: S1470-2045(18)30675-2. doi: 10.1016/S1470-2045(18)30675-2. [Epub ahead of print]

Background

Glioblastoma is a highly vascularised tumour and there are few treatment options after disease recurrence. Regorafenib is an oral multikinase inhibitor of angiogenic, stromal, and oncogenic receptor tyrosine kinases. We aimed to assess the efficacy and safety of regorafenib in the treatment of recurrent glioblastoma.

Method

REGOMA is a randomised, multicentre, open-label phase 2 trial done in ten centres in Italy. Eligible patients (aged ≥ 18 years) with histologically confirmed glioblastoma, Eastern Cooperative Oncology Group performance status 0 or 1, and documented disease progression after surgery followed by radiotherapy and temozolomide chemoradiotherapy were randomly assigned (1:1) by a web-based system, stratified by centre and surgery at recurrence (yes vs no), to receive regorafenib 160 mg once daily for the first three weeks of each four-week cycle or lomustine 110 mg/m² once every six weeks until disease progression, death, unacceptable toxicity, or consent withdrawal. The primary endpoint was overall survival in the intention-to-treat population. This trial is registered with ClinicalTrials.gov, NCT02926222, and is currently in follow-up.

Findings

Between 27 November 2015 and 23 February 2017, 124 patients were screened and 119 eligible

patients were randomly assigned to receive regorafenib (n=59) or lomustine (n=60). Median follow-up was 15.4 months (IQR 13.8-18.1). At the analysis cut-off date, 99 (83%) of 119 patients had died: 42 (71%) of 59 in the regorafenib group and 57 (95%) of 60 in the lomustine group. Overall survival was significantly improved in the regorafenib group compared with the lomustine group, with a median overall survival of 7.4 months (95% CI 5.8-12.0) in the regorafenib group and 5.6 months (4.7-7.3) in the lomustine group (hazard ratio 0.50, 95% CI 0.33-0.75; log-rank p=0.0009). Grade 3-4 treatment-related adverse events occurred in 33 (56%) of 59 patients treated with regorafenib and 24 (40%) of 60 with lomustine. The most frequent grade 3 or 4 adverse events related to regorafenib were hand-foot skin reaction, increased lipase, and blood bilirubin increased (in six [10%] of 59 patients each). In the lomustine group, the most common grade 3 or 4 adverse events were decreased platelet count (eight [13%] of 60 patients), decreased lymphocyte count (eight [13%]), and neutropenia (seven [12%]). No death was considered by the investigators to be drug-related.

Interpretation

REGOMA showed an encouraging overall survival benefit of regorafenib in recurrent glioblastoma. This drug might be a new potential treatment for these patients and should be investigated in an adequately powered phase 3 study.



READ IT BEFORE
YOUR PATIENTS

TRIALS

Characteristics of radiotherapy trials compared with other oncological clinical trials in the past 10 years

Liu X, Zhang Y, Tang LL, Le QT, Chua MLK, Wee JTS, Lee NY, O'Sullivan B, Lee AWM, Sun Y, Ma J

JAMA Oncol. 2018;4(8):1073-1079. doi:10.1001/jamaoncol.2018.0887

Importance

Modern precision radiotherapy is an innovative and effective treatment of cancer, yet it is unclear how radiotherapy trials are affected by expanding targeted and immune therapies and declining National Institutes of Health funding.

Objective

To analyse and compare the characteristics of radiotherapy trials with other oncological trials registered on ClinicalTrials.gov.

Design, setting, and participants

This is a cross-sectional analysis of trials registered on ClinicalTrials.gov between 1 June 2007 and 8 May 2017. Records of all 243,758 clinical studies registered by 8 May 2017 were downloaded, but only 25,907 interventional oncological trials registered between 1 June 2007 and 8 May 2017, and whose primary purpose was 'treatment' were included in the final analysis. Trials were categorised according to cancer type and other registration information.

Main outcomes and measures

Characteristics of radiotherapy trials were compared with characteristics of other oncological trials. Chronological shifts in radiotherapy trials were also analysed.

Results

Of the 25,907 trials selected, 1,378 (5.3%) were radiotherapy trials and 24,529 (94.7%) were other oncological studies. The number of radiotherapy trials increased gradually from 94 (1 June 2007 through 31 May 2008) to 192 (1 June 2015 through 31 May 2016). Radiotherapy trials were less likely than other oncological studies to be registered before participant enrolment (763 of 1,370 [55.7%] vs 16,105 of 24,434 [65.9%]; $P < .001$), to be blinded (45 of 1,378 [3.3%] vs 2,784 of 24,529 [11.3%]; $P < .001$), or to involve multiple geographic regions (2.4% vs 9.5%; $P < .001$), but they were more likely to be phase 2 to 3 (773 of 1,124 [68.8%] vs 12,910 of 22,300 [57.9%]; $P < .001$) and to have a data-monitoring committee (839 of 1,264 [66.4%] vs 11,728 of 21,060 [55.7%]; $P < .001$). Only a minority of radiotherapy trials were industry sponsored, which was significantly lower than for other oncological trials (80 of 1,378 [5.8%] vs 10,651 of 24,529 [43.4%]; $P < .001$; adjusted odds ratio, 0.08; 95% CI, 0.06-0.10). The number of National Institutes of Health-sponsored radiotherapy trials decreased from 80 of 544 trials (14.7%) from 2007 to 2012 to 72 of 834 trials (8.6%) from 2012 to 2017 ($P < .001$). Radiotherapy trials with a sample size of more than 100 patients decreased from 155 of 543 trials (28.5%) from 2007 to 2012 to 157 of 833 trials (18.8%) from 2012 to 2017 ($P < .001$).

Conclusions and relevance

The limited number of and the scarcity of ▼

funding for radiotherapy trials is concerning given the integral role of radiotherapy in the clinical management of patients with cancer worldwide. A multidisciplinary collaboration to promote and fund more radiotherapy research is warranted.





READ IT BEFORE
YOUR PATIENTS

RADIOSENSITIVITY

Papaverine and its derivatives radiosensitise solid tumours by inhibiting mitochondrial metabolism

Benej M, Hong X, Vibhute S, Scott S, Wu J, Graves E, Le QT, Koong AC, Giaccia AJ, Yu B, Chen SC, Papandreou I, Denko NC

Proc Natl Acad Sci U S A. 2018 Oct 16;115(42):10756-10761. doi: 10.1073/pnas.1808945115. Epub 2018 Sep 10.

Abstract

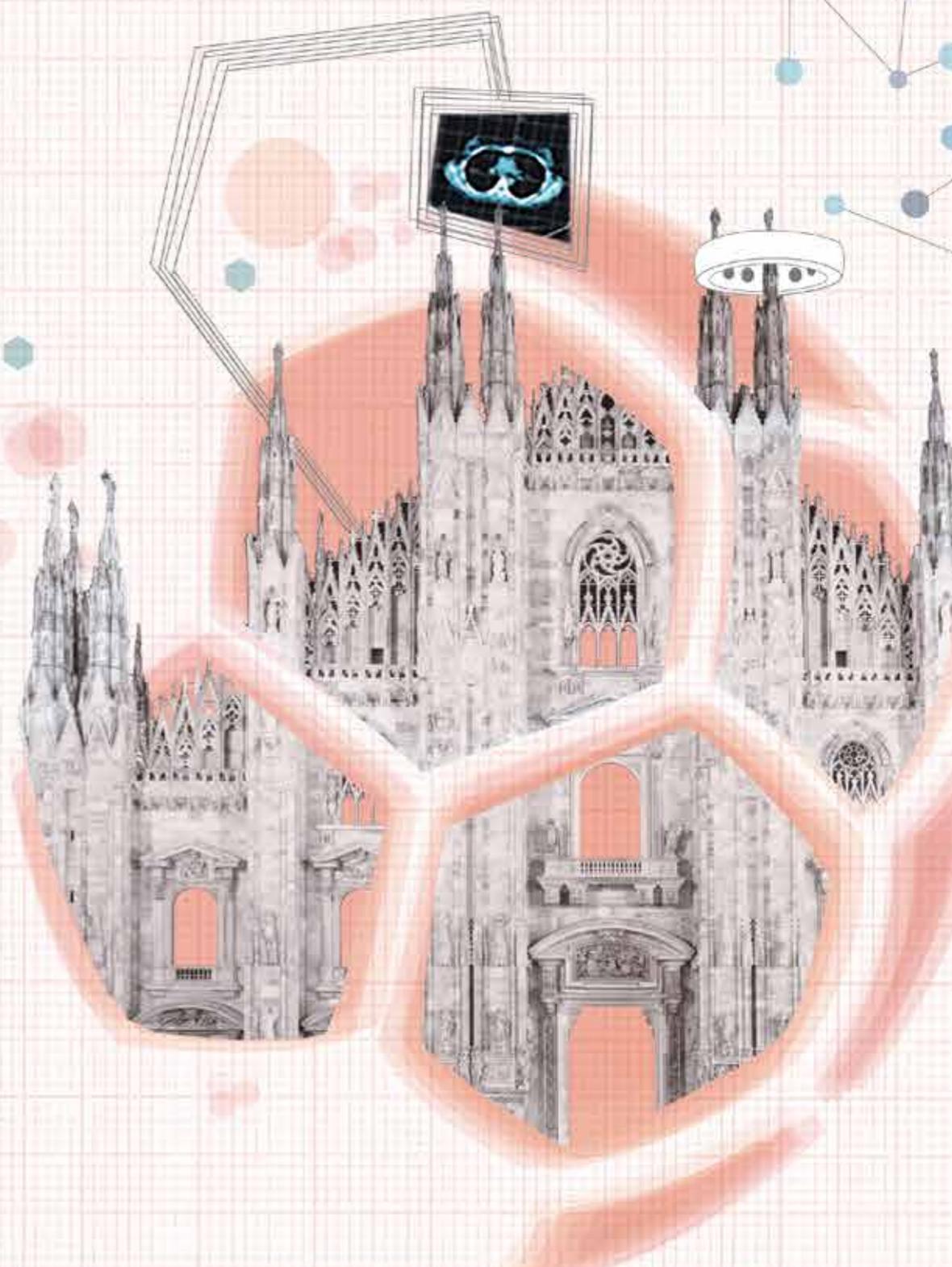
Tumour hypoxia reduces the effectiveness of radiation therapy by limiting the biologically effective dose. An acute increase in tumour oxygenation before radiation treatment should therefore significantly improve the tumour cell kill after radiation. Efforts to increase oxygen delivery to the tumour have not shown positive clinical results. Here we show that targeting mitochondrial respiration results in a significant reduction of the tumour cells' demand for oxygen, leading to increased tumour oxygenation and radiation response. We identified an activity of the FDA-approved drug papaverine as an inhibitor of mitochondrial complex I. We also provide genetic evidence that papaverine's complex I inhibition is directly responsible for increased oxygenation and enhanced radiation response. Furthermore, we describe derivatives of papaverine that have the potential to become clinical radiosensitisers with potentially fewer side effects. Importantly, this radiosensitising strategy will not sensitise well-oxygenated normal tissue, thereby increasing the therapeutic index of radiotherapy.





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BRACHYTHERAPY

—

“This edition of the Brachytherapy Corner covers a wide range of issues reflecting the extensive activity in the discipline across ESTRO”

—



GEC-ESTRO ASSEMBLY

Saturday 27 April
13:30-14:30 | Room Brown 2

ESTRO 38, Milan

This edition of the Brachytherapy Corner covers a wide range of issues reflecting the extensive activity in the discipline across ESTRO. The sixth GEC-ESTRO workshop was held in Brussels, Belgium, in November 2018 with the theme ‘Performing optimal brachytherapy’. We open this issue with two reports on this highly successful meeting.

The activity within GEC-ESTRO revolves around the working groups. In this issue we have an update from the head and neck working group, highlighting an important development – the establishment of two sub-groups for skin and eye tumours respectively. As always, readers who have an interest in these areas of brachytherapy are encouraged to get in touch with the group leaders and contribute to the group’s activities.

The editors’ choice from the literature highlights three papers: two on brachytherapy for cervical cancer, describing experience with interstitial brachytherapy using a new applicator, the third from the EMBRACE group, reporting the transition from Point A doses to volume-based doses, which is becoming the standard defined in ICRU 89. This is a brave attempt to unravel the controversy over whether low dose rate (LDR) or high dose rate (HDR) brachytherapy is better for localised prostate cancer, using a propensity matched analysis of published data. Read on if you want to know the answer.

We also have a review of a new book ‘Emerging technologies in brachytherapy’, which was co-edited by two prominent members of GEC-ESTRO. With contributions from more than a hundred experts this is a *tour de force*, which will bring readers abreast of current and future thinking in brachytherapy.

Finally, and with great sadness, we learnt of the death of Janusz Skowronek in December 2018. He had been a great supporter of GEC-ESTRO, serving on the committee and as a member of UROGEC. An appreciation of his life and contributions closes this Corner.

Peter Hoskin, Bradley Pieters, Åsa Tedgren



PETER HOSKIN



BRADLEY PIETERS



ÅSA CARLSSON
TEDGREN



Report on 6th GEC-ESTRO workshop, “Performing optimal brachytherapy”

Clinician's perspective ▶▶

by Viktor Smanykó

Physicist's perspective ▶▶

by Shrikant Kale

Report on 6th GEC-ESTRO workshop, “Performing optimal brachytherapy”

29-30 November 2018
Brussels, Belgium



VIKTOR SMANYKÓ

CLINICIAN'S PERSPECTIVE

The sixth Groupe Européen de Curiethérapie (GEC)-ESTRO workshop was held on 29-30 November in Brussels, Belgium. The theme of the workshop was “Performing optimal brachytherapy”. Almost every working group was represented.

BRAPHYQS (BRachytherapy PHYSics Quality Assurance System)

During this session a new model-based dose calculation was presented. It was interesting to hear about the liquid-filled ionisation chamber array, which is more accurate in measuring dose than standard semiconductor diodes.

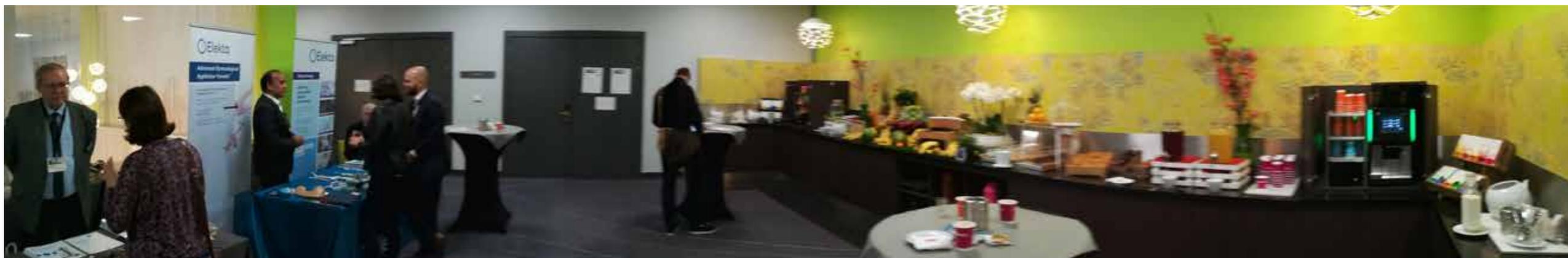
UroGEC

Carl Salembier's presentation showed that low dose rate (LDR) prostate brachytherapy can be safely performed after transurethral resection as long as modern imaging and optimised dosimetry techniques are used. The second part of this session dealt with the question of salvage brachytherapy after previous external beam radiotherapy, using high dose rate (HDR) or low dose rate (LDR) techniques. After excluding the presence of distant metastases and histological



Carl Salembier presenting during UroGEC Post TURP and Salvage session

confirmation of recurrence, we can treat just the affected part of the prostate or the seminal vesicle, while sparing surrounding normal tissues, which reduces the undesirable effects of repeated radiation therapy. This treatment results in better local control with fewer side effects than standard salvage prostatectomy. ▼



Exhibition and coffee area

Anorectal and skin

In this session the topic was the feasibility of rectal brachytherapy as a boost after external beam radiotherapy with 50kV contact X-ray (Papillon) technique (OPERA trial) or HDR intra-luminal technique (HDREBT trial) for elderly patients who usually are not fit for or keen to undergo major surgery. The second part of this session showed that brachytherapy has favourable cosmesis over teletherapy for skin cancer, as we saw in the SCRiBE meta-analysis. Furthermore, new 3D-printing applicators enable efficient individualised treatment.

Breast

In this part of the workshop the speakers presented an ESTRO guideline on delineation

for accelerated partial breast irradiation after closed and open cavity surgery. We also watched an educational video on how to execute CT-guided implantation in practice. Jean-Michel Hannoun-Levi showed new results confirming that second breast conserving surgery with perioperative HDR interstitial brachytherapy is a safe and feasible option for the management of ipsilateral breast tumour recurrence, resulting in similar five-year oncologic outcomes compared to standard salvage mastectomy.

Gynaecological

A retrospective study on brachytherapy in medically inoperable endometrium cancer was presented, which found large heterogeneity between the centres. We also learned that if

MR is not available for treatment planning, we can achieve similar results with the use of contrast-enhanced CT and ultrasound guidance implantation in cervix cancers. Finally, we discussed EMBRACE recommendations for treatment planning.

All the speakers and participants thought that the sixth GEC-ESTRO workshop was a success. The next workshop will be held on 21-22 November 2019.

*Viktor Smanyakó
National Institute of Oncology
Centre of Radiotherapy
Budapest, Hungary ▼*

PHYSICIST'S PERSPECTIVE

The sixth GEC-ESTRO workshop was held in Brussels, Belgium, in November 2018. Thanks to the organisers and the team in the ESTRO head office, the 192 participants from 28 countries experienced a well-organised and structured scientific programme, as well as warm hospitality.

The theme of the workshop was 'Performing optimal brachytherapy'. The sessions were dedicated to the ESTRO working groups: BRAPHYQS, UroGEC, anorectal and skin, breast, and gynaecological. The central message of the workshop was that brachytherapy should not be done only as a job, task or duty. Instead it should always be as accurate as possible and delivered at an outstanding level with absolute commitment. The chair of GEC-ESTRO, Bradley Pieters, welcomed all participants and speakers.

BRAPHYQS

This session was strongly driven by a need for guidelines on commissioning of treatment planning systems (TPS) used for brachytherapy and for pre-treatment quality assurance procedures. We discussed the set of tests that

need to be performed for TPS commissioning. The importance of moving towards model-based algorithms for brachytherapy dose calculation and their validation was emphasised. Also discussed was the need for pre-treatment quality assurance (QA) in brachytherapy using different types of detectors to be confident about the accuracy of dose delivery.

UroGEC

This session started with a talk on the rationale and outcomes of prostate brachytherapy after transurethral resection of the prostate (TURP). It also included a literature review. This was followed by indications for salvage brachytherapy in the prostate, and techniques and optimal imaging requirements. At end of the session, we discussed clinical outcomes of salvage prostate brachytherapy.

Anorectal and skin

In this session, we discussed indications and techniques for optimal brachytherapy for rectal cancers. There was an interesting talk on measures to reduce toxicities in cases of rectal ▼



SHRIKANT KALE

brachytherapy and on X-ray brachytherapy for rectal cancers, along with techniques and clinical outcomes.

The skin session emphasised the need for an interdisciplinary approach in order to establish brachytherapy as a major treatment modality for treatment of skin cancers in the 21st century (ironic given that the first attempt to use radiation for clinical treatment 100 years ago was in relation to the skin).

In the talk on the pitfalls of skin brachytherapy planning, there was concern about a lack of consensus guidelines on brachytherapy of skin cancers, dose prescriptions, and consideration of involved organs at risk and their tolerances. We also discussed the steps being taken to formulate ESTRO skin working group recommendations and an online atlas for skin brachytherapy cases.

Breast

In this session, we discussed the guidelines for target definition and delineation for accelerated partial breast irradiation (APBI) after closed- and open-cavity breast conserving surgery. There was a video presentation on CT-guided implantation for breast brachytherapy. We also discussed the ESTRO / advisory committee on

radiation oncology practice (ACROP) guidelines for breast brachytherapy. The work group results of a multicentre study on 'Second conservative treatment for second breast tumour events' were presented. There was healthy discussion on contouring, and dose volume evaluation of accelerated partial breast irradiation.

Gynaecological

This session focused on brachytherapy in endometrium cancer and upcoming GEC-ESTRO recommendations for cervix cancer treatment. Matthew Harkenrider highlighted the US guidelines for brachytherapy in medically inoperable endometrium cancer. This was followed by a presentation of the results and outcomes of the GEC-ESTRO retrospective study on brachytherapy in medically inoperable endometrium cancer. It was concluded that guidelines were needed to reduce heterogeneity in treatment approaches and to improve patient management. In the later part of the session there was an overview of GEC-ESTRO/IBS (India Brachytherapy Society) recommendations on CT-based contouring in cervix cancer. We also discussed the GEC-ESTRO recommendations on treatment planning, plan analysis and reporting.

The workshop concluded with some remarks

from the chair-elect of the GEC-ESTRO committee, Ina Jurgenliemk-Schulz. The eminent speakers and enthusiastic participants made this event a great success.

Shrikant Kale
Medical physicist
Department of Medical Physics
Tata Memorial Hospital
Dr Ernest Borges Road, Parel,
Mumbai, India



Head & neck and skin GEC-ESTRO working group 2018 report

The head & neck and skin GEC-ESTRO working group consists of a core group of 23 members from several European and Asian countries. The group is currently undertaking a range of research, clinical practice and education projects. To maximise efficiency two specific task groups (eye, led by Luca Tagliaferri and skin, led by Jose Luis Guinot) were created as part of the working group.

The main aims of the working group are to propose and organise research projects for the creation of clinical evidence and to improve the quality of patient treatments by defining uniform protocols, especially in the fields of implant and quality assurance (QA) procedures, image-guided radiotherapy, 3D treatment planning, dose prescription, and dose constraints for organ at risk evaluation.

Research projects

The working group's main research project is COBRA¹ (Consortium for BRachytherapy data Analysis). The COBRA consortium is an international research network for interdisciplinary standardised data collection in the field of head and neck, skin and eye brachytherapy, made up of 15 international institutions. It uses a dedicated web-based platform to share clinical data, which can be used for both retrospective studies and prospective research trials.



LUCA TAGLIAFERRI

The COBRA-Storage System (C-SS) guarantees patient privacy and is efficient to use. Thanks to its use of 'brokers', data can be extracted directly from a single centre's storage systems through a connection with a 'structured query language database'. The C-SS also benefits from 'distributed learning' approaches, in which data never leave the collecting institution, while learning algorithms and proposed predictive models are commonly shared².

All projects start with the creation of a site-specific ontology (advanced data-set) that is used by all participants. The objectives of the project are to facilitate the management of prospective trials, and to create predictive clinical models for supporting physicians in their clinical practice by evaluating the response and the toxicity probability of a given treatment. There are several COBRA projects underway, the main ones being retrospective studies on nose and oropharynx cancer treatments and a prospective trial on skin basal cell carcinoma. All interested international groups with large mono-institutional retrospective databases are invited to join these projects.

Clinical practice activities

In order to homogenise clinical practice, several members are involved in writing relevant chapters of the second edition of the GEC-ESTRO *Handbook of Brachytherapy*³ and the site-specific GEC-ESTRO/ACROP ▼

recommendation papers. In recent years, two endorsed guidelines for head and neck, and skin have been published in *Radiotherapy & Oncology*: in 2017 the first update of head and neck brachytherapy in squamous cell carcinomas recommendation⁴, and in 2018 the skin brachytherapy guidelines⁵, with a focus on 3D imaging-based treatment planning and stepping source technology.

In relation to clinical practice activities, the ‘How to treat’ project started recently. This has entailed the production of several practical teaching videos accompanied by documents for the various cutaneous or head and neck sites, useful for those who want to improve their clinical practice by observing the procedures performed and commented on by experienced members of the working group. The main objectives are: to provide tips and suggestions for troubleshooting solutions in the implant procedure; to create a common language for dose prescription; to advise on adequate methods for personalised dose distribution and organs at risk (OaR) evaluation; and to identify EQD2 minimal dose values to the target and EQD2 constraints for the OaR.

Educational activities

The working group is committed to educational issues, and many of its members are involved in several international teaching activities. The most important in this field are the ESTRO course on ‘Multidisciplinary management of

non-melanoma skin cancer’ and the GEC-ESTRO-endorsed multidisciplinary course on head and neck. In addition, in cooperation with national societies, several group members are regularly participating in different on-site educational events. In order to facilitate the educational activities in head and neck brachytherapy, especially for young physicians, the group recently approved a postgraduate residents exchange project among member institutions. Several working group members also presented on brachytherapy topics at ESTRO 37 in Barcelona and at the first ‘ESTRO meets Asia’ conference in Singapore.

The working group was well represented at the recent GEC-ESTRO workshop in Brussels, with members discussing some of the state-of-the-art developments in ongoing and future working group projects.

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www.gemelliart.it

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- [2] ENT COBRA ONTOLOGY: the covariates classification system proposed by the Head & Neck and Skin GEC-ESTRO Working Group for interdisciplinary standardized data collection in head and neck patient cohorts treated with interventional radiotherapy (brachytherapy). Tagliaferri L, Budrukkar A, Lenkowicz J, Cambeiro M, Bussu F, Guinot JL, Hildebrandt G, Johansson B, Meyer JE, Niehoff P, Roviroso A, Takácsi-Nagy Z, Boldrini L, Dinapoli N, Lanzotti V, Damiani A, Gatta R, Fionda B, Lancellotta V, Soror T, Monge RM, Valentini V, Kovács G. *J Contemp Brachytherapy*. 2018
- [3] <https://www.estro.org/about/governance-organisation/committees-activities/gec-estro-handbook-of-brachytherapy>
- [4] GEC-ESTRO ACROP recommendations for head & neck brachytherapy in squamous cell carcinomas: 1st update – Improvement by cross sectional imaging based treatment planning and stepping source technology. Kovács G, Martinez-Monge R, Budrukkar A, Guinot JL, Johansson B, Strnad V, Skowronek J, Roviroso A, Siebert FA; GEC-ESTRO Head & Neck Working Group. *Radiother Oncol*. 2017
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Combined intracavitary and interstitial brachytherapy of cervical cancer using the novel hybrid applicator Venezia: clinical feasibility and initial results ▶▶

High-dose-rate brachytherapy monotherapy versus low-dose-rate brachytherapy with or without external beam radiotherapy for clinically localised prostate cancer ▶▶

Isodose surface volumes in cervix cancer brachytherapy: change of practice from standard (Point A) to individualised image-guided adaptive (EMBRACE I) brachytherapy ▶▶

Combined intracavitary and interstitial brachytherapy of cervical cancer using the novel hybrid applicator Venezia: clinical feasibility and initial results

Walter F, Maihöfer C, Schüttrumpf L, Well J, Burges A, Ertl-Wagner B, Mahner S, Belka C, Gallwas J, Corradini S.

Brachytherapy. 2018 Sep - Oct;17(5):775-781. doi: 10.1016/j.brachy.2018.05.009. Epub 2018 Jun 22.



FRANZISKA WALTER



STEFANIE CORRADINI

What was your motivation for initiating this study?

Standard treatment of locally advanced cervical cancer includes external beam radiation therapy (EBRT), concomitant chemotherapy, and, importantly, brachytherapy (BT) of the primary tumour. Based on the Groupe Européen de Curiethérapie (GEC)-ESTRO recommendations, the implementation of MR-guided brachytherapy is crucial for improving tumour control and the incidence of adverse effects. Image-guided adaptive brachytherapy (IGABT) requires MR imaging of the tumour on the day of treatment with an MR-compatible brachytherapy applicator in place. This allows for the optimal assessment of tumour shape and extension. However, precise tailoring of dose distribution to larger or irregular shaped tumours is challenging and often requires the addition of interstitial (IS) to conventional intracavitary (IC) brachytherapy.

There are several recent technical solutions for combining interstitial and intracavitary (IS/IC) brachytherapy in one hybrid applicator. Our clinic was among the first institutions in the world to implement the Venezia™ applicator (Elekta, Sweden) into routine clinical practice. In fact, we performed the first in-human treatment using this applicator in March 2017. We wanted

to report on the first clinical results and designed a planning study comparing this technique to previously applied methods.

What were the main challenges during the work?

In the article we reported on the initial clinical experience of a technique, previously not applied in our institution. Implementing a new technique in your clinical routine is challenging in many ways. In the case of the Venezia™ applicator, it opened the door to performing MR-guided IGABT for patients with cervical cancer. We had to design a completely new workflow, including brachytherapy pre-planning, an exact imaging schedule, accurate patient preparation (e.g. bladder and bowel filling regimen, and sufficient pain management), an agreed approach to inserting the applicator, and treatment planning and dose delivery. The main challenge after this was to report our findings in a timely manner, while at the same time securing a reasonable amount of expertise to support our findings. ▼

What are the most important findings of your study?

For this study we conducted a plan comparison of the clinically applied IS/IC brachytherapy versus conventional point A, and manually optimised IC plans, both using only the ring/tandem components of the hybrid applicator. For comparison, we evaluated parameters of dose delivery to the target volume, as well as planning aims for organs at risk. Target volume delineation and dose constraints were applied according to GEC-ESTRO recommendations. A clear benefit was shown for the treatment plan using the full scope of the hybrid applicator, both in dose coverage of the target volume and the sparing of organs at risk. This benefit was seen in the comparison of median doses between the respective plans. We decided to visualise the results for each individual patient. In a scoring system each case was evaluated for dose coverage and organ sparing. Using the IS/IC plans, all but two plans achieved full scores, while the point A plans and the IC plans reached full scores in only one and three cases, respectively, therefore delivering less optimal plans for the majority of patients.

What are the implications of this research?

Besides showing the feasibility of combined IS/IC brachytherapy using the Venezia™ applicator with IGABT, we were able to conduct a plan comparison using well-established techniques, namely the prescription to point A and a manually optimised plan with the use of only tandem and ring. We think this research is important because it clearly illustrates the benefits to the patient of using this new technical solution over conventional and widely used methods. Given the additional expense in terms of time, money and workforce costs of IGABT over a more simple point A plan, it is well worth making this comparison. We believe our findings positively visualise how the implementation of modern techniques can translate into a benefit for the individual patient. We hope it will encourage other institutions to integrate this technology into their clinical practice.

*Franziska Walter and Stefanie Corradini
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“WOMEN IN MEDICAL PHYSICS - MEET AND GREET”

Sunday 28 April
08.00-09.00 | Open space area of Exhibition

PHYSICS ASSEMBLY

Monday 29 April
13:30-14:30 | Room Brown 1

ESTRO 38, Milan

High-dose-rate brachytherapy monotherapy versus low-dose-rate brachytherapy with or without external beam radiotherapy for clinically localised prostate cancer

Yamazaki H, Masui K, Suzuki G, Nakamura S, Yamada K, Okihara K, Shiraishi T, Yoshida K, Kotsuma T, Tanaka E, Otani K, Yoshioka Y, Ogawa K

Radiother Oncol. 2018 Nov 8. pii: S0167-8140(18)33544-8. doi: 10.1016/j.radonc.2018.10.020. [Epub ahead of print]



YAMAZAKI HIDEYA

What was your motivation for initiating this study?

We started using high-dose-rate brachytherapy (HDR-BT) monotherapy in the 1990s and low-dose-rate brachytherapy (LDR-BT) with or without external beam radiation therapy (EBRT) in the 2000s. This is a reversal of what happened in prostate brachytherapy worldwide, where LDR-BT was adopted initially and then HDR-BT was explored later. We thought that HDR-BT could be used to treat not only low to intermediate risk groups, but also high-risk groups with androgen deprivation therapy (ADT). LDR-BT has been regarded as a one of the standard modalities for treating low to intermediate risk groups. Subsequently it was used as a boost treatment for high-risk groups treated with EBRT. Now, we are faced with the difficulty of which is the better modality to recommend to patients, when both have similar eligibility criteria. Therefore, we decided to compare these modalities to establish which is the better treatment option.

What were the main challenges during the work?

We found that there was a huge selection bias between HDR-BT and LDR-BT. HDR-BT is

used to treat more advanced disease than LDR-BT. Therefore, we introduced a new statistical method (inverse probability of treatment weighting (IPTW) involving propensity scores) to reduce this selection bias. Although it could not replace a randomised controlled trial, we believe it is the best way to achieve as fair comparison as possible at present.

What are the most important findings of your study?

The actuarial five-year biochemical failure-free survival rates (bNED) were 100% and 97.3% ($p = 0.99$) in the low-risk groups for HDR-BT and LDR-BT respectively; 95.6% and 94.3% ($p = 0.19$) in the intermediate risk groups; and 93.1% and 94.9% ($p = 0.98$) in selected high-risk groups, excluding T3b-4 and initial PSA ≥ 50 . IPTW correction also indicated no difference in bNED between LDR-BT and HDR-BT groups. LDR-BT showed a higher incidence of genitourinary (GU) toxicity grade ≥ 2 than HDR-BT in the acute phase and grade one toxicity in the late phase. The accumulated incidence of late grade ≥ 2 GU and GU toxicity was equivalent between HDR-BT and LDR-BT. No grade 4 or 5 toxicities were detected in either modality. ▼

What are the implications of this research?

Both LDR-BT and HDR-BT are excellent treatment options for appropriately selected patients, with comparable outcomes and acceptable toxicities. Therefore, physicians and patients can choose either treatment confidently, depending on its availability and their preferences.

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7 GEC ESTRO workshop

21-22 November 2019
Budapest, Hungary

DEADLINES

Early registration:
19 September 2019

Late registration:
until 07 November 2019

Registrations close:
07 November 2019 at 12:00 CET.

On-site registration will NOT
be available

Isodose surface volumes in cervix cancer brachytherapy: change of practice from standard (Point A) to individualised image-guided adaptive (EMBRACE I) brachytherapy

Serban M, Kirisits C, Pötter R, de Leeuw A, Nkiwane K, Dumas I, Nesvacil N, Swamidas J, Hudej R, Lowe G, Hellebust TP, Menon Gio, Oinam A, Bownes P, Oosterveld B, De Brabandere M, Koedooder K, Marthinsen ABL, Lindegaard J, Tanderup K; EMBRACE Collaborative Group.

Radiother Oncol. 2018 Dec;129(3):567-574. doi: 10.1016/j.radonc.2018.09.002. Epub 2018 Sep 19.



MONICA SERBAN



CHRISTIAN KIRISITS



KARI TANDERUP

What was your motivation for initiating this study?

The concept of “dose at Point A” has been previously used as an indicator of the intensity of a brachytherapy (BT) treatment, but for combined intracavitary / interstitial (IC/IS) brachytherapy, Point A dose cannot be used for reporting due to the potential closeness of needles to Point A. For advanced image-guided adaptive brachytherapy (IGABT) using IC/IS implants, this direct comparison to Point A doses and long-term anchorage to previous clinical practice has therefore been missing.

The isodose surface volumes (ISVs) are based on the idea of the “60 Gy reference volume”, but are now expanded to cover different external beam radiation therapy (EBRT) and brachytherapy cumulative dose levels and to refer to both target and organs at risk (OARs). The ISVs are independent of contoured target volumes and are related to the dwell times, source strength and implant geometry. They can be regarded as indicators of treatment intensity and can be used to compare treatments within or across different institutions and EBRT / brachytherapy fractionation schedules.

This study reported on the size of the ISVs corresponding to 60 Gy, 75 Gy and 85 Gy EQD2 dose levels, from the radiobiological perspective of both tumour and normal tissue, for patients enrolled in the EMBRACE I study. A comparison of Point A standard loading and IGABT systems was conducted with the aim of showing how brachytherapy practice has evolved over time.

What were the main challenges during the work?

The main challenge was to investigate the most influential brachytherapy schools and their practice and evolution over the past century, in order to relate it to current IGABT practice in terms of ISVs and loading patterns. A second challenge was to study the effect of dose rate (pulsed dose rate versus high dose rate), EBRT dose and α/β ratio on the relative positioning and spacing between ISVs at 85 Gy, 75 Gy and 60 Gy EQD2 dose levels and to represent it concisely in a graphical form.

What are the most important findings of your study?

MR-IGABT and individualised dose prescription during EMBRACE I resulted in improved ▼

target dose coverage and decreased treated volumes compared to standard plans used with classical Point A-based brachytherapy. In 38% of EMBRACE patients, the V85 Gy was similar to standard plans with 75–85 Gy to Point A. In total, 41% of patients had V85 Gy smaller than standard plans receiving 75 Gy at Point A, while 21% of patients had V85 Gy larger than standard plans receiving 85 Gy at Point A. The ISVs depended strongly on high-risk clinical target volume, which demonstrates that dose adaptation was performed per individual tumour size and response during EBRT.

What are the implications of this research?

In addition to target and OARs dose-volume histogram (DVH) parameters, the ISVs could add to the understanding of risk factors for treatment-related toxicity and local disease failure. As such, the ISVs from the EMBRACE study could be used to add predictive power to normal tissue complication models, in addition to small volumes (e.g., D_{2cm^3}) irradiated to high doses and extracted from contoured OARs. The ISVs could also be used in centres that are not able to perform volumetric contouring and advanced treatment planning.

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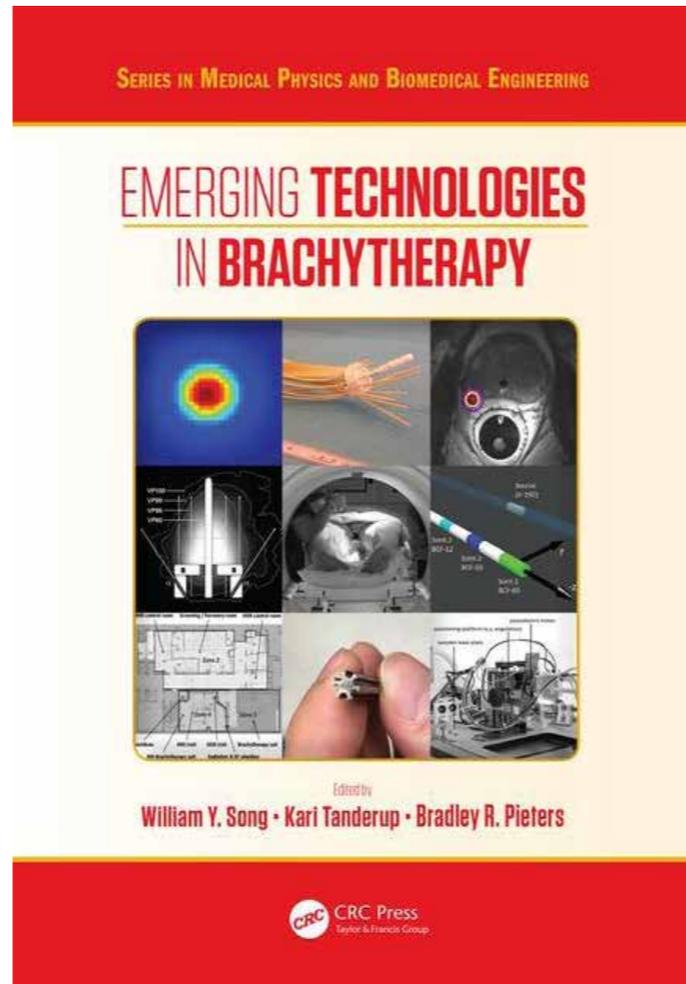
Physicists take part in the: Pattern Of Practice for Adaptive and Real Time Radiation Therapy (POP-ART RT) survey

More details in the Physics Corner on page 58 >

BOOK REVIEW

Emerging Technologies in Brachytherapy

William Y. Song, Kari Tanderup,
Bradley Pieters.
CRC Press, First edition, May 23, 2017



As implied by the title and clearly stated by the editors in the introduction, the aim of *Emerging Technologies in Brachytherapy* is to provide "... a concise collection of *emerging* technologies and trends in brachytherapy as well as the political / economic landscape in which these innovations must persist, on a global scale".

Boasting contributions from more than a hundred experts across 31 chapters, it is a real challenge to come up with an aspect of current, or near future, brachytherapy practice that is not discussed.

Besides being well thought out, the contents of the book are very efficiently arranged in five sections. The first two sections ('physics of brachytherapy' and 'imaging for brachytherapy guidance') are in essence a digest of literature from the past few years on innovative approaches and advances in the field, filtered by the expertise and experience of the contributors. Some material on the current standard of care in clinical practice is included, to a varying degree, in all chapters. This is justified by the need to set the stage as well as to highlight the most recent developments in each area.

All the chapters deliver on the aim of the book, and they do so with commendable features. For example, chapter 6 (dose optimisation) stands out for its completeness; the inclusion of separate chapters on image processing (chapter 7) and 3D printing in brachytherapy (chapter 11) is valuable; the inclusion of worked out examples in chapter 7 (failure mode and effects analysis (FMEA) for brachytherapy) livens up a subject deemed too administrative by some; chapter 9 (real-time *in vivo* dosimetry) succeeds in delivering a comparative analysis of proposed methods instead of simply listing them, and all the chapters on imaging in section II strike a perfect balance between current implementation and future perspectives.

Section III comprises an interesting collection of eight clinical sites demonstrating varying degrees of resources and clinical brachytherapy ▼



PANAGIOTIS
PAPAGIANNIS

programme development. This section is also valuable in terms of the open exchange of experience showing a sample of international programmes.

Section IV provides decisive arguments for the role of advanced brachytherapy in the armamentarium of a comprehensive radiotherapy setting, as well as its cost effectiveness.

Finally, Section V presents the industry perspective on what the near future has in store for brachytherapy.

Overall, this book fulfils its aim. Criticism can only be made on technicalities such as the inclusion of only two major vendors in the brachytherapy technology in section V, not referring to the potential cost of introducing some of the emerging technologies in clinical practice, or the fact that much of the material relates to emerging techniques rather than technologies.

One might even argue that most of the emerging technologies discussed comprise a technology-push, rather than a demand-pull.

Perhaps, however, there lies the main contribution of this book. It is an essential adjunct to books on the physics and clinical practice of brachytherapy that will help the multidisciplinary brachytherapy team member

delineate potential pitfalls and areas of further improvement in their clinical practice. Even if not all the technologies discussed make the transition to widespread clinical use, it will help teams to move forward with confidence, to the advantage of the field and, ultimately, patients.

Panagiotis Papagiannis
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IN MEMORY**Professor
Janusz Skowronek**



ADAM CHICHEL

Dear friends,

It is with great regret and sadness that we inform you of the death of Professor Janusz Skowronek, the Editor-in-Chief of the *Journal of Contemporary Brachytherapy* (JCB), on 20 December 2018.

For a number of years, Janusz had been struggling with health problems that finally overcame him. It is a great loss for us, the staff of the brachytherapy department in the Greater Poland Cancer Centre in Poznań, for the Centre itself, for the whole Polish radiotherapy community and also for all the makers and readers of the *Journal of Contemporary Brachytherapy*. Janusz Skowronek's creative mind, stubborn character and heroic work put JCB in the important place that it now occupies in the field.

Professor Janusz Skowronek was born in Poznań in 1964. Aged 19 he was diagnosed with Hodgkin lymphoma. After almost a year-long chemo- and radiotherapy programme, he was successfully cured. In 1983 he graduated from High School No 8 in Poznań and decided to become a physician. A year later he started his studies at the Medical Academy in Poznań, receiving his physician diploma in June 1990. He was recognised with a Medical Academy Medal for "Achievements in science and social work". Janusz defended his doctoral thesis in 1996 on the subject of "Assessment of DNA content in



malignant melanoma cells". Just one year later he passed his second degree examination for radiation oncology with merit. On 15 November 2006 he passed a postdoctoral examination (habilitation) on the subject of "Comparison of the effectiveness and the risk of complications after pulsed-dose rate brachytherapy (PDR) and high-dose rate brachytherapy (HDR) based on the biologically equivalent dose (BED) model". He was made a Professor in Medical Sciences on 4 March 2015, receiving this title from the President of Poland.

Janusz started his professional work in the radiotherapy department in the Greater Poland Cancer Centre in 1991. In 1997 he moved to the first radiotherapy ward at the same centre. Because of his great interest in brachytherapy, he led the work to set up a brachytherapy workroom, which opened on 1 June 2003. Two years later on 1 August 2005 a brand new ▼

brachytherapy department and brachytherapy ward were opened. From then on, he served as the head of the department. As an open-minded doctor with vision and ideas he gathered a group of doctors, physicists, technicians and nurses who all became devotees of brachytherapy under his well-organised team. Students and oncology residents will remember his interesting and practical lectures, which were well supported by practical demonstrations.

Over many years of work Janusz became a valuable member of numerous scientific societies: the Polish Oncologic Society (PTO, twice the past head of the regional branch), Polish Brachytherapy Society (PTB, head), Polish Radiation Oncology Society (PTRO), ESTRO, GEC-ESTRO committee member (2013-2018), URO-GEC group member, American Society for Therapeutic Radiology Oncology (ASTRO), American Brachytherapy Society (ABS), European Society for Hyperthermic Oncology (ESHO), and the Prostate Cancer Research Study Group (PCRSO).

The milestone of his accomplishments in the brachytherapy community was the *Journal of Contemporary Brachytherapy* – both the initial idea and its consistent realisation. The *JCB* was like a child to him, and he was devoted to it unconditionally. On 5 November 2008 Janusz became Editor-in-Chief of *JCB*. Soon after, its first issue 1/2009 vol. 1 was published, the first of another 48 issues. Janusz had been beaver-

ing away on the journal almost until the very end. One can find no words to do justice to his dedication.

Janusz's experience of oncologic treatment in adolescence had a huge impact on the rest of his life and health. The consequences of his mediastinal irradiation and cardiotoxic chemotherapy cast a ray of sunlight on his professional career and a shadow on his heart. News of his death in December from heart failure spread around the world quickly and was met with great sadness.

Professor Janusz Skowronek was buried on 4 January 2019 at Junikowo Cemetery in Poznań, Poland. He will endure in our loving memory... Farewell, Janusz!

Adam Chicheł
Brachytherapy department
Greater Poland Cancer Centre
Poznań, Poland



PHYSICS

“*Motion sickness and light flashes experienced by patients are not the type of topics you would expect to be covered in medical physics papers.*”



PHYSICS ASSEMBLY

Monday 29 April
13:30-14:30 | Room Brown 1

ESTRO 38, Milan

Dear colleagues,

Welcome to the Physics Corner. This edition starts with an article about the work of Blake Smith, a PhD student at the University of Wisconsin-Madison, USA, who has undertaken a research project on determining the scatter neutron dose originating from a dynamic collimating system. The dynamic collimating system has been put forward as a method to improve the conformity of the dose around the target during proton pencil beam scanning for intracranial lesions. Blake researched the scatter neutron dose and compared the results to traditional collimating systems.

Motion sickness and light flashes experienced by patients are not the type of topics you would expect to be covered in medical physics papers. Nevertheless, in this Corner we show why these phenomena are relevant to patients.

Alexander Jöhl evaluated motion sickness and body motion experienced during dynamic couch tracking, a process used to compensate respiratory motion of the tumour. He recruited 100 volunteers to undergo the procedure. The aim of the work was to quantify the body motion induced by the couch movements and to investigate whether the volunteers experienced any motion sickness. You can read about the results in the interview with Alexander.

One of the intriguing effects of irradiation is the light flashes seen by some patients during their treatment. This phenomenon, known technically as ‘visual phosphenes’, has recently been investigated by Willy de Kruijff and colleagues. They looked for factors that impact the occurrence of visual phosphenes. In this Corner, Willy de Kruijff explains what they found.

We also want to draw your attention to a new institutional survey on the ‘Pattern of practice for adaptive and real time radiation therapy’ (POP-ART RT). The survey has been created by participants from the 2nd ESTRO physics workshop held in Spain last October. The survey invites departments to answer questions on their use of gating/tracking for respiratory motion management, and of adaptive radiotherapy using multiple treatment plans for the management of interfraction motion.

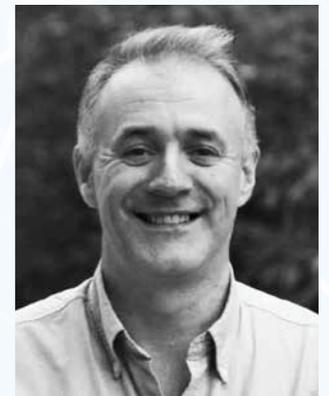
As usual, we welcome any feedback on the Physics Corner. We also invite you to offer your suggestions for PhD research, back-to-school topics, and other subjects for forthcoming Corners.

We look forward to meeting as many of you as possible at ESTRO 38.

Mischa Hoogeman (m.hoogeman@erasmusmc.nl),
Brendan McClean (Brendan.McClean@slh.ie),
Christian Richter (christian.richter@oncoray.de)



MISCHA HOOGEMAN



BRENDAN MCLEAN



CHRISTIAN RICHTER

Secondary neutron dose from a dynamic collimation system during intracranial pencil beam scanning proton therapy: a Monte Carlo investigation ▶▶

Body motion during dynamic couch-tracking with healthy volunteers ▶▶

Occurrence and mechanism of visual phosphenes in external beam radiation therapy and how to influence them ▶▶



Secondary neutron dose from a dynamic collimation system during intracranial pencil beam scanning proton therapy: a Monte Carlo investigation

Smith BR, Hyer DE, Hill PM, Culberson WS

Int J Radiat Oncol Biol Phys. 2019 Jan 1;103(1):241-250.
DOI: 10.1016/j.ijrobp.2018.08.012. Epub 2018 Aug 14



BLAKE R SMITH

What was your motivation for initiating this study?

The dynamic collimation system is an experimental collimator that is capable of energy-layer specific collimation through the sequenced motion of collimation trimmers. Recently, there has been a growing interest in the development and application of these dynamic collimators in pencil beam scanning proton therapy (PBS) in order to improve the target conformity of the treatment, especially for lower-energy treatments, such as intracranial brain tumours.

One feature of these devices is that they are placed in close proximity to the patient in order to minimise the degree of beam scatter and divergence in the air prior to reaching the patient. However, a caveat to this approach is the presence of a potential neutron source in close proximity to the patient from the nuclear interactions that occur in the range shifter and collimators. While the reduction of secondary neutron production was considered in the material choice of the trimmers, it was not immediately clear what influence the system would have on secondary neutron production and the exposure to the patient.

What were the main challenges during the work?

There is a substantial amount of literature that has investigated secondary neutron production and dose rates from a variety of passive scattering and uniform scanning systems. However, the neutron dose rates estimated from these studies are rather difficult to compare, since these studies collectively report using several different radiation exposure quantities and utilise a wide range of experimental methods or Monte Carlo techniques.

Another challenge was evaluating the secondary neutron production from the dynamic collimation system in a clinically relevant scenario. This required an extensive geometric modelling of the treatment CT-planning dataset in a Monte Carlo radiation transport code, MCNP6. To simulate the entire treatment plan, each beamlet needed to be individually simulated, which required extensive organisation of computational resources.

What is the most important finding of your study?

The secondary neutron exposures from the incorporation of a dynamic collimation ▼

system appear to be less than those estimated for uniform scanning treatments with brass apertures. This was mainly due to the differences in collimating materials. The trimmers of the dynamic collimation system are composed of nickel, which has a smaller neutron production rate than brass or tungsten. Additionally, only a portion of the peripheral beamlets interact with the trimmers, whereas a portion of a brass aperture may be used to block an incident field of protons scanned over a large area.

What are the implications of this research?

Dynamic collimation has the potential to spare a larger amount of healthy tissue and to increase target conformity for low-energy PBS proton therapy treatments. The presence of the collimation trimmers did increase the secondary neutron dose rates compared to an uncollimated treatment. However, when you take into account the secondary neutron effects during treatment, our results indicate that the degree of healthy tissue sparing from the primary proton beam outweighs the risk from the neutrons produced in the collimators.

Blake R Smith

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Medical Radiation Research Center
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5th European Particle Therapy Network (EPTN)

9 April 2019 | Brussels, Belgium

REGISTRATION IS OPEN!

www.estro.org/congresses-meetings/items/5th-european-particle-therapy-network-eptn



New series on PhD research in the Physics Corner

Have you just completed or are you about to complete an interesting PhD thesis?

Then please share it with the ESTRO physics community by contacting Christian at christian.richter@oncoray.de for more details. If your report is accepted by the editors of the Physics Corner, it will be published in a forthcoming issue of the newsletter.

Body motion during dynamic couch-tracking with healthy volunteers

Jöhl A, Bogowicz M, Ehrbar S, Guckenberger M, Klöck S, Meboldt M, Riesterer O, Zeilinger M, Schmid Daners M, and Tanadini-Lang S

Physics in Medicine and Biology 64(1) November 2018

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ALEXANDER JÖHL



STEPHANIE TANADINI-LANG

What was your motivation for initiating this study?

Respiratory-induced tumour motion during radiotherapy treatments adversely affects the desired dose distributions and leads to larger target margins being used. Motion mitigation techniques such as respiratory gating or dynamic tracking of the tumour position enable you to reduce the tumour margins. One method of achieving this is 'couch-tracking', in which the patient is continually moved to compensate for the tumour motion.

However, a major concern of couch-tracking is that the patient's body might move during the treatment. Another concern is that the patient could experience motion sickness and might not tolerate this motion. We wanted to establish that these are minor issues before we set up a clinical trial with patients. In order to do this we performed a clinical study with volunteers, evaluating the body motion and the motion sickness for 100 healthy volunteers. In this sub-study we report on the results of the induced body motion due to tracking.

What were the main challenges during the work?

From writing the ethics proposal to finishing

the evaluation took us three years in total. There were many challenges along the way. In order to make valid statements, we needed a large number of volunteers. We recruited 100 volunteers in total, which was a major challenge. We went to many events to present our study and to recruit volunteers, including for example, events held by the Senior Citizens' University based at Zurich University.

Each study day we had to make sure that all sub-systems were running properly. The evaluation of the body motion on our in-house-developed couch-tracking system using an in-house-developed surface scanner was only one part of the study. The other was to evaluate volunteer reaction and motion sickness during tracking. For this, we measured heart rate, respiratory frequency, skin humidity and eye motion. We had five sub-systems, which had to be set up and synchronised before each measurement session because the study was performed on a clinical accelerator, which was used for patient treatments the rest of the day.

Another challenge was the data evaluation. We placed multiple markers on the patient and combining this information with the volunteers' body motion was more difficult than we ▼

expected. For example, we had to subtract the respiratory motion to find what motion was really induced by the couch motion.

What is the most important finding of your study?

We found that the volunteers were very stable on the couch during couch-tracking. The median-induced couch motion was ten times smaller compared to the breathing motion. The largest body motion was in longitudinal direction, with lateral and vertical directions of similar magnitude. A small number of volunteers experienced a larger motion (up to 3 mm), but for all volunteers the reduction in tumour motion due to couch-tracking was significantly larger compared to the induced body motion. We did an additional test of the couch with a chirp signal (2cm sinus motion, which increases the frequency over time), instead of the volunteers' respiratory motion. For that signal, we found a slightly increased body motion (median 1.2mm, max 3.2mm) compared to the respiratory tracking tests, probably due to the larger motion and the higher frequency of the signal.

What are the implications of this research?

Ideally, couch-tracking would allow the size of the target volume to be as if the tumour was static. However, the couch motion induces a small additional body motion, which increases the uncertainty of the tumour position. Therefore, the increase in uncertainty would have to be met by an increase of the target volume to be treated. The results of our work allow an estimate of the magnitude of necessary target volume increase.

The induced motion was small. As such, the couch tracking approach reduces the overall tumour position uncertainty significantly. These are encouraging results on the way to implementing couch-tracking in a clinical trial. These results are also promising for other techniques requiring the couch to move during the treatment, such as 4pi treatments.

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GEC-ESTRO ASSEMBLY

Saturday 27 April
13.30-14.30 | Room Brown 2

“WOMEN IN MEDICAL PHYSICS - MEET AND GREET”

Sunday 28 April
08.00-09.00 | Open space area of Exhibition

ESTRO 38, Milan

Occurrence and mechanism of visual phosphenes in external beam radiation therapy and how to influence them

Kruijf W, Timmers A, Dekker J, Böing-Messing F, Rozema Ta

Radiation and Oncol. Volume 132, March 2019, Pages 109-113

DOI: 10.1016/j.radonc.2018.11.010



WILLY DE KRUIJF

What was your motivation for initiating this study?

Visual phosphenes are flashes of light and other unusual visual phenomena seen by patients during their radiation therapy treatment, which many patients find unpleasant. This study started with a question from a radiation oncologist at Instituut Verbeeten about whether we understood why a patient experienced these phosphenes when they were treated with a particular treatment machine, but did not experience them when they were treated with another. Because there were multiple patients with similar complaints, we ruled out possible dosimetric differences and then decided to investigate the occurrence of these visual phosphenes in general. Subsequently, a radiation therapist's PhD thesis study revealed that a difference existed between a particular treatment machine and other treatment machines. Because the illuminance in this particular treatment room is lower than in other treatment rooms, we hypothesised that the difference in occurrence of visual phosphenes is caused by the difference in illuminance level. We initiated a new study in which we randomly varied the illuminance in one treatment room and asked patients about their experiences with visual phosphenes.

Another personal motivation is that these visual phosphenes are very intriguing. In the early years after the discovery of radioactivity they were already known and studied, and they received new attention after the first flights into space, because astronauts also experienced these visual phosphenes.

What were the main challenges during the work?

Visual phosphenes occur during irradiation and we expect them to be dependent on dose rate rather than dose. A challenge, which we have not solved, is that we cannot calculate the time-dependent dose rate to specific tissues in volumetric modulated arc therapy (VMAT) treatments. We use dose as a surrogate for dose rate in our statistical model.

Another challenge was to build an understanding of the physical and biological mechanism of these visual phosphenes. We decided to investigate both the occurrence of light flashes, probably associated with direct activation of photoreceptor proteins in the retina, and the occurrence of steady light, probably associated with the Cherenkov radiation generated in the vitreous humour. ▼

The difference between the two phenomena might be difficult to notice for patients, especially because they may appear together.

What is the most important finding of your study?

The most important finding of our study is the conclusion that the complaints of our patients can be explained by the low illuminance level in the particular treatment room. Furthermore, we show a dependence of visual phosphenes on dose.

What are the implications of the research?

With this study we contribute to a better understanding of the phenomenon of visual phosphenes. Moreover, we have identified parameters (dose rate, illuminance) that can be used to reduce the probability of visual phosphenes.

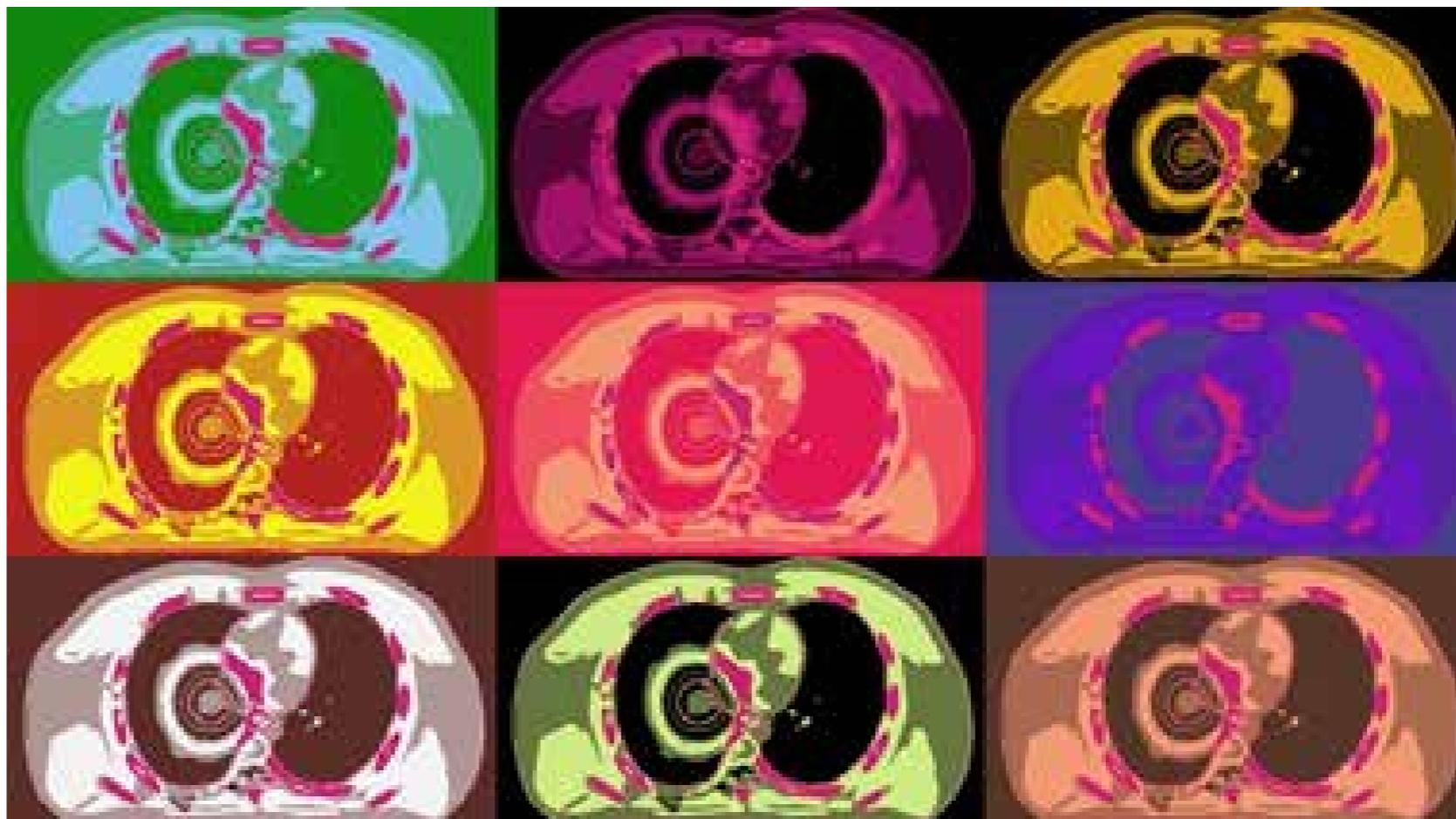
Apart from the photoreceptor proteins of the rods and cones in the retina, melanopsin was indicated as a photoreceptor possibly involved in visual phosphenes. Melanopsin was discovered

in 1998 and is involved in the circadian rhythm. We hypothesise that fatigue could be related to visual phosphenes, which would increase the clinical relevance of reducing the occurrence of these visual phosphenes. Further research is needed to confirm or reject such a relationship.

*Willy de Kruijf
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Pattern Of Practice for Adaptive and Real Time Radiation Therapy (POP-ART RT)



The Pattern Of Practice for Adaptive and Real Time Radiation Therapy (POP-ART RT) study has been established by participants of the "real-time and adaptive management of anatomical variations" track at the 2nd ESTRO physics workshop, held in October last year in Málaga, Spain.

The study has two aims. First, we would like to determine to what extent and how adaptive and real-time radiotherapy is being used in clinical practice. Second, and more importantly, we

would like to understand what the barriers to implementation or further use are.

Therefore, we have developed an institutional survey, which contains questions on the current use of gating/tracking for respiratory motion management, and for adaptive radiotherapy using multiple treatment plans for the management of interfraction motion. The survey also contains questions on plans for further or new implementation of real-time and adaptive motion management techniques, and the main



JENNY BERTHOLET GAIL DISTEFANO BEN HEIJMEN MARIANNE AZNAR

barriers and challenges preventing wider use.

It is important for the success of this study that all institutions complete the survey, including those that are not doing any form of adaptive or real-time radiotherapy. For those institutions where this is the case, the survey will only take five minutes to complete.

The results, which we intend to disseminate through a scientific paper, will enable us to identify the necessary action to be taken by vendors, users and society to implement adaptive and real-time radiation therapy more widely in clinical practice and to increase confidence in using this new technology.

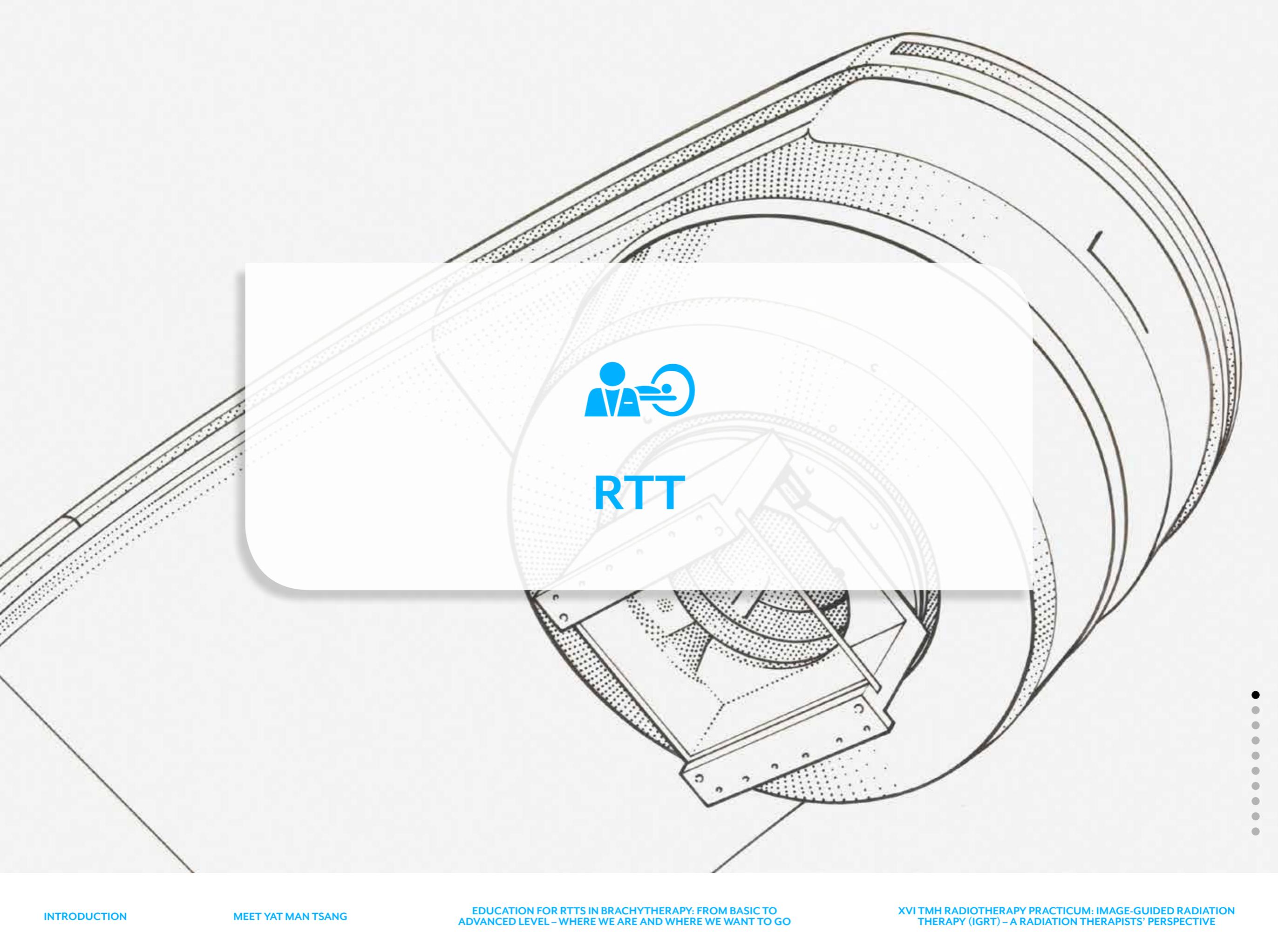
We hope you find this project interesting and valuable, and that you can find time to coordinate with your colleagues to provide one answer to the survey per institution. We thank you in advance for your participation and look forward to sharing the results of the POP-ART RT study with you.

Please complete the survey online at: www.surveymonkey.co.uk/r/RZRYF83 A PDF of the survey is also downloadable (https://www.estro.org/binaries/content/assets/pdf/projects/pop-art_rt.pdf) and can be used for internal discussion before completing the online form.

If you would like more information, please email: Gail Distefano (gail.distefano@nhs.net) or Jenny Bertholet (jenny.bertholet@icr.ac.uk).

On behalf of the POP-ART RT workshop participants, Jenny Bertholet, Gail Distefano, Ben Heijmen and Marianne Aznar





RTT



“The RTT Corner features three pieces, each addressing the importance of education in improving patient care”

Welcome to this edition of the RTT Corner, which features three pieces, each addressing the importance of education in improving patient care.

Dr Yat Mang Tsang, of Mount Vernon Cancer Centre, London (UK), shares his experience of gaining a PhD through a publication award. He describes the extensive research experience he has gained working within the national Radiotherapy Trials Quality Assurance (RTTQA) group and as a consultant practitioner. He highlights how this experience, paired with good mentorship, has led to a successful research career.

Bernd Wisgrill, an RTT working in the General Hospital Vienna (Austria), reports on the educational requirements of an RTT specialising in brachytherapy. Bernd describes how RTTs have become more involved in the multidisciplinary team and the patient pathway, which means there is a greater need for specialised education.

Maeve Kearney, of Trinity College Dublin (Ireland) and George Biju, from the Tata Memorial Hospital, Mumbai (India), report on the first ESTRO-endorsed image-guided radiation therapy (IGRT) course for RTTs in India. This course allowed RTTs the opportunity to learn from lectures and hands-on sessions that aimed to address the gap in IGRT training and to standardise practice throughout the country.

We would like to thank all contributors who have kindly shared their experiences in this edition. Please get in touch if you have any comments or suggestions for future newsletters, by email or in person at ESTRO 38.

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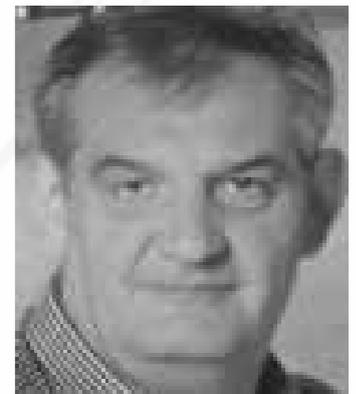
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ILIJA ČURIĆ

Meet Yat Man Tsang: an RTT and clinical- academic specialising in clinical trials quality assurance



YAT MAN TSANG

It's my great pleasure to have this opportunity to talk about my career journey as a radiation therapist (RTT). After the excellent career path articles written by my peers Mirjam Mast and Rita Simoes in the previous newsletter, this task has become more difficult. I hope the readers of the ESTRO RTT Corner will enjoy reading about my career development.

My early career

In 2002, I obtained my BSc in radiotherapy at the Hong Kong Polytechnic University. My interest in radiotherapy dosimetry arose from my original BSc thesis, which compared the dose distribution from a tailor-made wax compensator and a universal aluminium compensator in the head and neck region for total body irradiation. It involved the use of thermoluminescent dosimeters for *in vivo* measurements and the construction of phantoms.

My first job as an RTT was in the Mount Vernon Cancer Centre (MVCC), which is based in the East and North Hertfordshire NHS Trust, in the UK. This position consolidated my professional knowledge and clinical experience within radiotherapy. In 2003, I began to pursue the academic part of my career and enrolled on an MSc degree in Healthcare Informatics and Technologies at City University, University of London. The degree provided a holistic approach to healthcare technology comprising seven modules: healthcare computing; healthcare data analysis; imaging for radiotherapy; operating

systems and networking; research methods; total quality management; and healthcare database and electronic patient records. My MSc dissertation involved the implementation of a database solution for interim quality assurance (QA) data analysis for a clinical breast trial. This opened the door to the world of clinical trials QA. I was appointed as a trial QA RTT within the national Radiotherapy Trials Quality Assurance (RTTQA) group in 2006.

Career progression into clinical trials QA

This appointment as the trial QA RTT has given me entirely new opportunities for research and development. I have become a clinical and technical expert in advanced radiotherapy technology, and now design and implement QA programmes for clinical trials that require the effective introduction of advanced radiotherapy in UK centres. This has equipped me with the skills and experience to contribute and support new ways of working within UK radiotherapy centres, ensuring staff have the necessary levels of competency and education required in the trials. This has also included collaborative work with other UK radiotherapy experts to develop training programmes for radiographers, physicists and clinicians.

Working as a consultant practitioner in radiotherapy

In 2014, I decided to take on a more clinical role and progressed to my current job as a consultant practitioner in radiotherapy at MVCC. ▼



Yat Man Tsang accepting his PhD

Across radiotherapy services, there has been national acknowledgement that the radiography career progression model, including the highest level of practice at consultant level, should be introduced across radiotherapy centres to meet local service need. For my consultant practitioner role, I act as both a clinical and technical expert to lead and coordinate the strategic planning of the NHS Trust's specialised radiotherapy service, including stereotactic radiotherapy. I am responsible for delivering and developing the technical standards for the radiotherapy service at MVCC. As the first radiotherapy consultant practitioner accredited by the Society and College of Radiographers (SCoR) in the UK, I always demonstrate my experience and expertise in the

four core functions through clinical practice, professional leadership and consultancy, research and education.

It is essential for RTTs to be research active. In 2015, the SCoR launched their new five-year strategy for research with an ambitious expectation that one per cent of the UK radiographer workforce would hold, or be working towards, a doctoral-level award by 2021. The strategy recommended that this expectation should apply to all consultant practitioners in radiotherapy. Through my previous trials QA work, I have been heavily involved in the national development of changes in fractionation for breast cancer and the clinical implementation of advanced radiotherapy within the UK. The SCoR's vision inspired me to carry out a PhD by published work and help to develop and fulfil my consultant practitioner role.

PhD by published work

In July 2018, I completed my PhD by published work with the title "Development of evidence-based practice in advanced radiotherapy through clinical trials quality assurance" at London Southbank University. The PhD by published work is a doctorate thesis comprised of sole- or multi-authored works that have been submitted or accepted for publication. It offers an alternative route to the award of a doctorate, but in all other regards must meet the standards for a traditional PhD.

This doctorate thesis has provided evidence to answer the research question of whether there is a role for trials QA in influencing the development of evidence-based practice in advanced radiotherapy. The evidence is found in my publications covering:

- Development of a national dosimetry audit programme in advanced radiotherapy
- Development of evidence-based practice by utilising trial radiotherapy planning dosimetry data
- Implementation of advanced radiotherapy through radiotherapy trials QA.

The critical evaluation analysis included in the thesis has demonstrated my achievements in influencing and advancing our profession as an RTT through establishing new QA standards in radiotherapy, and providing UK centres with a strong cooperative network and a safe environment for implementing new advanced radiotherapy techniques.

My plans for the future

In the UK, there is a need for the development of a formal career pathway for all non-medical healthcare professionals who have the ability and desire to pursue a clinical-academic career. It is exactly this type of career path that I am very happy to be moving into. I am also working closely with my local universities to support post-registration training and education for RTTs. In terms of my research profile, ▼

I am involved in numerous national trial management groups and the National Cancer Research Institute Clinical and Translational Radiotherapy Research Working Group. All of these activities will hopefully strengthen my position as a health research leader and consolidate my clinical-academic career prospects.

Acknowledgements

First, I would like to express my sincere gratitude to my clinical mentors Professor Peter Hoskin, Dr Karen Venables and Mrs Jagdeep Kudhail, for their continuous support of my career and research work.

Besides my mentors, I would also like to thank my doctorate thesis supervisors at London South Bank University: Dr Adele Steward-Lord and Dr Martin Benwell, for their insightful comments and encouragement, and also for their criticisms and suggestions, which motivated me to widen the scope of my research.

I am also grateful to Professor John Yarnold, Dr Charlotte Coles and Dr Catharine Clark who provided me with access to their research facilities and data. Without their precious support it would not have been possible for me to establish my research career.

Finally, I would like to thank my colleagues and friends at Mount Vernon Cancer Centre. In

particular, I am grateful to the RTT QA group for providing me with my first stepping stone into research and for their stimulating discussions.

*Yat Man Tsang | PhD
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See the course report on “Positioning and immobilisation for radiotherapy” by Filipa Sousa

[School Corner on page 86 >](#)



Read the “MOBILITY REPORT Radiomics assessment of radiation-induced parotid gland changes” by Elizabeth Forde, an RTT

[More details in the Young Corner on page 99 >](#)

Education for RTTs in brachytherapy: from basic to advanced level – where we are and where we want to go



BERND WISGRILL

Teletherapy and brachytherapy are the mainstays of radiotherapy in treating malignant diseases.

Although brachytherapy offers very good results in the treatment of gynaecological tumours, breast cancer, prostate cancer and head and neck tumours, it plays a relatively minor role compared to teletherapy, especially in the western world.

Due to the very good results, many clinics provide brachytherapy. However, there are considerable differences in the complexity of the treatments performed. For the most part, clinics undertake simple therapy methods. However, some specialised centres offer highly complex interstitial, image-supported brachytherapy, which requires a lot of planning. As such, the requirements for their staff and their training are also different. Here, I would like to consider specifically the role of radiation therapists (RTTs) in this process.

The European Higher Education Area level 6 (EHAH l6) benchmarking document, published in 2014, defines the competencies that RTTs should have on graduation from their basic education programme. It is recommended that RTT training meets the EHAH l6 benchmarking document, including the European Qualifications Framework level 6 (EQF l6), which is equivalent to the level of an undergraduate bachelor's degree. By default, the EQF is divided into the 'Knowledge, Skills,

and Responsibility and Autonomy', which an employee in a department should have. At level 6, it is assumed that an employee will have advanced knowledge in the subject area (Knowledge), be able to find answers to questions themselves (Skills) and be responsible for actions that lie within their scope of duties.

The scope of the RTT is defined by the International Atomic Energy Agency (IAEA) as follows: "They are the professionals with direct responsibility for the daily administration of radiotherapy to cancer patients. Depending on local policy, this may include treatment preparation and planning, treatment delivery, clinical and psychosocial care of the patient on a daily basis during treatment and immediate post-treatment review" (*A handbook for the education of radiation therapists* (RTTs) IAEA, 2014).

The brachytherapy section of EQF L6 conforms to this role and recommends basic training, including various brachytherapy techniques, evaluation of treatment plans and dose parameters, treatment of patients, adherence to specific radiation protection, as well as equipment handling and the preparation of the irradiation room.

The curricula of the universities that train RTTs are by and large adapted to these recommendations. However, the dominance of teletherapy means that more time is spent ▼

training in this field. Brachytherapy is reduced to the basics and is not taught so thoroughly. For the majority of clinics where brachytherapy plays a subordinate role, this is sufficient, but specialised centres place higher demands on the capabilities of RTTs. Complex brachytherapy requires multidisciplinary cooperative work between all the professional groups involved, in which all participants must communicate on the same level. Like teletherapy, brachytherapy is also subject to constant change and progress, driven by scientific research across the professional groups. These circumstances change the role of the classic RTT profile and bring new challenges. RTTs are taking more responsibility for aspects of treatment and new areas of activity. It is essential that RTTs who undertake advanced roles or a greater level of responsibility are trained to a very high standard to ensure that patients receive safe and accurate treatment.

Against this background, the RTT brachytherapy team at the general hospital in Vienna, Austria, created a survey to identify the necessary skills and knowledge, which was presented at ESTRO 38. We analysed the clinical workflow of image-guided adaptive brachytherapy for cervix cancer, with all the tasks for RTTs documented and the required skills and knowledge itemised. This detailed evaluation revealed that in relation to documentation, imaging, treatment planning and treatment delivery, RTTs require skills and knowledge in anatomy, medical physics, brachytherapy-specific medical engineering,

nursing and workflow coordinating that go beyond basic RTT skills.

This is where the recently published European Higher Education Area levels 7 and 8 postgraduate benchmarking document for RTTs comes in. This document is designed to help universities to develop radiation therapy-specific curricula for postgraduate education to prepare RTTs for advanced roles. Here the skills and competencies previously defined at level 6 serve as a base, with levels 7 and 8 setting out the skills and competencies needed for delivering more advanced brachytherapy.

Level 6 states that the RTT must understand the basic principles of brachytherapy. Levels 7 and 8 require the RTT to be an autonomous member of the team who participates in all aspects of the procedures, including patient preparation, pre-treatment imaging, treatment delivery, follow-up and all related health and safety procedures. At level 8 the RTT should also play a more active role in the management of brachytherapy.

In the past, the necessary skills and knowledge were acquired either on the job within the clinic itself or through further education received on an external programme. This created long training phases for new employees and a heterogeneous level of knowledge among RTTs.

The goal for the future in brachytherapy must be that we offer all RTTs university-level

postgraduate education and standardised further education, which are valid internationally. This is essential to adapt the role of RTTs to the new requirements of radiotherapy. The European Higher Education Area levels 7 and 8 postgraduate benchmarking document for RTTs provides all the necessary information for the preparation of a sufficient postgraduate education.

The success of this approach hinges on the willingness of universities to adapt the curricula, offer new postgraduate training and to communicate with therapy centres to respond to new demands.

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XVI TMH Radiotherapy Practicum: image-guided radiation therapy (IGRT) – a radiation therapists’ perspective

15-16 September 2018, Tata Memorial Hospital, Mumbai, India



XVI TMH Radiotherapy Practicum ‘IGRT-A radiation therapists’ perspective’

Image-guided radiation therapy (IGRT) has revolutionised radiation therapy in cancer care, with technological developments driving rapid change. Nowhere have the advances in IGRT been more evident than in the role of the RTT. Educational curriculums and continuous training of RTTs is essential to enable autonomous professions to execute a successful IGRT workflow. One of the ESTRO School’s aims is to promote international exchange of knowledge and experience in the field of radiotherapy and oncology. This year, a dedicated RTT training course in India received full endorsement from the ESTRO School for the first time. I was privileged to represent the ESTRO School at the event.

There are one million cases of cancer diagnosed in India each year (1). India is a low-middle-income country with a large population (1.3 billion) and landmass spread across 29 states. This brings with it huge diversity and heterogeneity on the ground, including in the professional field of RTTs. More than 300 centres provide radiotherapy services across the country, of which the majority are either government-funded academic institutions or non-academic institutions. There are also privately funded non-academic institutions, but fewer private academic centres. There is a large pool of trained RTTs (approximately 1,400-1,500), 90% of whom are registered with the Association of Radiation Therapy Technologist of India (ARTTI), the main professional body representing RTTs in ▼



MAEVE KEARNEY



GEORGE BIJU



XVI TMH RTT team of Tata Memorial Hospital, Mumbai

the country. Like Europe, India has seen huge leaps in IGRT development in recent years and budget allocation towards cancer-specific care has increased from 115 million Indian rupees in 1980 to 60,000 million Indian rupees in recent budgets (2).

The XVI TMH Radiotherapy Practicum: 'IGRT – a radiation therapists' perspective' took place from 15-16 September 2018 in Tata Memorial Hospital, Mumbai. The practicum consisted of a number of lectures and practical hands-on demonstrations. Registration was limited to 60 participants and only open to RTT professionals with access to IGRT facilities. The practicum coincided with the Hindu festival of Ganesh Chaturthi, which celebrates the birthday of Lord Ganesh. Lord Ganesh is a symbol of wisdom, prosperity and good fortune and the holiday is a

day of devotion. Despite falling during a period of reverence, attendance at the practicum was at full capacity.

Lung, cervix and head and neck cancers are most prevalent across India (2). Consequently, there was a special emphasis on these sites within the context of the lectures covering IGRT modalities, workflow, verification considerations and motion-management strategies. After each session, there was a period for questions and discussion that enabled all delegates to share common issues they have encountered, and which led to many lively discussions.

As the host centre, Tata Memorial was represented strongly on the programme delivering interesting presentations on their workflow and practices, particularly in relation to departmental motion-management procedures for breast and lung cancer.

Tata Memorial is a Varian-based site boasting a Novalis TX, TrueBeam, Trilogy and a Tomotherapy HiArt accelerator among its facilities. 4D-CT is also routine practice. This provided an ideal location for the demonstration component of the practicum.

There are 34 institutes offering RTT educational programmes across India, at diploma, BSc and MSc levels. The duration of these programmes vary and the usual training programme comprises two years training (at level 1-2) with

a one-year compulsory internship. The Atomic Energy Regulatory Board (AERB) regulates all courses. The formal education entry level is high school, either at 12th grade or bachelor's in science (preferably physics).

New graduates enter at a 'junior technologist' level, where the focus is on building competencies and confidence in routine radiotherapy practice. Gradually junior technologists progress and become clinically competent in advanced techniques, progressing to level 8, following 8-15 years experience to become a 'chief technical officer'. In non-academic centres, role progression is less structured and remuneration is based on years of experience rather than clinical skills.

As the delegation size was small, I was able to speak to many of the delegates and faculty members over the duration of the practicum. Among RTTs, there are huge variances in IGRT practices, with some displaying a degree of apprehension regarding volumetric imaging. Some new graduates also begin their professional training at peripheral centres that lack the most up-to-date radiotherapy technologies. This may be the reason for inconsistencies in IGRT application across India, which was also evident in results from the pre-course questionnaire completed by attendees.

There is an unmet need for training in advanced technology, such as IGRT, adaptive ▼

radiotherapy, stereotactic radiotherapy etc, for a broad base of RTTs. Most of the older generation of RTTs are not exposed to these technologies, yet years of service can be the main basis for career progression in their centre. The compartmentalisation of RTTs to ‘simulation’ and ‘treatment delivery’ is also commonplace, with little focus on producing integrated RTTs who are fully competent in both areas. Radiotherapy departments, in general, do not have well-established planning to treatment workflow and lack systematic quality assurance programmes.

However, intellectual curiosity, enthusiasm and motivation to drive progress were very evident among the RTTs. The desire for regular training of this type was reiterated throughout the weekend. India is a vast country with a large, strong RTT presence. Increased investment in continuous professional development should be part of increasing IGRT facilities. There is a glaring lacuna in programmes for continuing education, training and retraining of RTTs at the local and national level.

A highly skilled workforce will maximise IGRT facilities providing world-class radiotherapy services to the Indian population.

Many thanks to Dr Rahul, Mr George Biju and all the RTTs at Tata Memorial, who were so hospitable over the course of the practicum. I look forward to returning someday.

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RTT ALLIANCE MEET AND GREET

Sunday 28 April
**10.30-11.30 | Open space area
of Exhibition**

RTT MEET AND GREET

Monday 29 April
**12.00-13.00 | Open space area
of Exhibition**

ESTRO 38, Milan





RADIOBIOLOGY



“*The most striking aspect of immunotherapy is that it targets cancer by activating the host’s immune system, rather than directly targeting the tumour*”

One of the most spectacular additions to the three standard treatments for cancer – radiotherapy, surgery and chemotherapy/targeted therapy – is immunotherapy. The most striking aspect of immunotherapy is that it targets cancer by activating the host’s immune system, rather than directly targeting the tumour. For a number of decades we know from a limited number of case reports that a tumor response can occur outside the radiation field. They were first defined by RH Mole in 1953 (*BrJ Radiol*) in the paper ‘An action at a distance from the irradiated volume but within the same organism’. In 2017, S Dovedi suggested an update for the definition in ‘Systemic anti-tumour *immune* responses outside of the irradiated tumour field’ (*Clin Canc Res*). With the emerging possibility of combining radiotherapy with immunotherapy on a larger scale, this is an interesting time for radiobiologists (D Schaeue and WH McBride, *Nat Rev Clin Oncol*. 2015). In this Radiobiology Corner we want to draw your attention to several papers published recently that have focused on combining immunotherapy and radiotherapy, which have been published outside the main journals that most of us read.



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Radboud University Medical Centre Nijmegen
The Netherlands*



**RADIOBIOLOGY MEET
AND GREET**

**Saturday 27 April
12:00-13:00 | Open space area of
Exhibition**

ESTRO 38, Milan



Heskamp S *et al.* PD-L1 microSPECT/CT imaging for longitudinal monitoring of PD-L1 expression in syngeneic and humanised mouse models for cancer

Heskamp S, Wierstra PJ, Molkenboer-Kuenen JDM, Sandker GW, Thordardottir S, Cany J, Olive D, Bussink J, Boerman OC, Dolstra H, Aarntzen EHJG, Hobo WA.

Cancer Immunol Res. 2019 Jan;7(1):150-161.

It is well established that blocking the interaction between programmed death ligand 1 (PD-L1) and PD-1 can have a strong therapeutic effect on small groups of patients. More interesting, if combined with chemotherapy or ablative therapies, the efficacy can be increased. However, we need to improve the selection of patients who are most likely to respond to these treatments. Heskamp *et al* have investigated the possibility of visualising and quantifying the PD-L1 expression using microSPECT/CT imaging. For this, they used several syngenic mouse tumour models. By doing so in a longitudinal way, they were able to show how tumours upregulate these proteins in response to, for instance, radiotherapy (see figure 6 in the article). As a result, we can now expect the development of a technique that will enable us to select patients for PD-1/PD-L1-targeted therapy using imaging. Potentially, the technique of longitudinal assessment of the PD-L1 developed by Heskamp *et al* may predict the efficacy of this treatment for individual patients. Interestingly, in the meantime this group has successfully translated this technique to cancer patients.

*Jan Bussink MD, PhD
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JAN BUSSINK



—

Radiotherapy and CD40 activation separately augment immunity to checkpoint blockade in cancer

Rech AJ, Dada H, Kotzin JJ, Henao-Mejia J, Minn AJ, Twyman-Saint Victor C, and Vonderheide RH

Cancer Res; 78(15) August 1, 2018

—



TONKE
RAAIJMAKERS

The abscopal effect, in which the immune system is activated so that it can clear distant metastases, is a mode of action all oncologists would like to achieve. Within the radiotherapy field, the effect has only occasionally been observed and documented. Additional immunotherapies are now explored (and applied) to achieve this desired effect. Immunotherapies can activate the immune system, or remove immune blockades that prevent the induction of an army of cytotoxic CD8+ T cells that can travel to distant sites. However, for pancreatic ductal adenocarcinoma (PDA), a type of cancer with a five-year survival of less than 10%, immunotherapy has not yet been effective.

Overcoming immunosuppressive barriers in PDA requires coordinated targeting of innate and adaptive immunity. In this paper, Rech *et al* show that the combination of radiotherapy with an anti-CD40 antibody, and dual immune checkpoint blockade (anti-CTLA-4/anti-PD-1) eradicates irradiated and unirradiated tumours (abscopal effect), generating long-term immunity in a PDA mouse model. Radiotherapy triggered an early activation of antigen-presenting cells and anti-CD40 caused systemic and intratumoural reorganisation of the myeloid compartment. Furthermore, the dual immune checkpoint blockade increased the intratumoural T cell infiltration, with a positive bias towards CD8+ T cells.

As such, this paper provides a rationale for the combination of radiotherapy with anti-CD40, and the immune checkpoint blockades anti-CTLA-4/anti-PD-1, in human PDA.

Tonke Raaijmakers
PhD student, ROI lab
Department of Radiation Oncology
Radboud University Medical Centre
Nijmegen, The Netherlands



Subjugation of TGFβ signalling by human papilloma virus in head and neck squamous cell carcinoma shifts DNA repair from homologous recombination to alternative end joining

Liu Q, Ma L, Jones T, Palomero L, Pujana MA, Martinez-Ruiz H, Ha PK, Murnane J, Cuartas I, Seoane J, Baumann M, Linge A and Barcellos-Hoff MH

Clinical Cancer Research, 2018. DOI: 10.1158/1078-0432.CCR-18-1346 published December 2018



EVA-LEONNE
GÖTTGENS

Over the last few years, it has become apparent that a one-size-fits-all approach for the treatment of head and neck squamous cell carcinomas (HNSCC) is not the best approach. Specifically, types of HNSCC that are caused by infection and integration with the oncogenic human papillomavirus (HPV) have been demonstrated to have a significantly improved response to radiation therapy. Multiple research groups have shown that this is, at least in part, related to the decreased DNA damage repair capacity of HPV+HNSCC, which explains their relatively high radiosensitivity.

This recent paper by Liu *et al* describes the role of transforming growth factor beta (TGF-β) in the repair deficiency of HPV+HNSCC. TGF-β is a cytokine that is mainly known for its importance in immune cell signalling and acts on B- and T-lymphocytes and macrophages. Liu *et al* have demonstrated that HPV+HNSCC tumours lack TGF-β signalling, and that this correlated with improved patient survival as well as cellular sensitivity to radiation. The proposed mechanism is based on their observation that TGF-β inhibits miR-182, and subsequently FOXO3 and BRCA1, impairing both DNA damage sensing as well as DNA damage repair via homologous recombination. As a result, these cells are more dependent on the more error-prone non-homologous end joining pathway, and therefore also susceptible to PARP inhibition.

This paper not only strengthens the theory that HPV+HNSCC have impaired DNA damage repair, but also links a key immunological factor to classical DNA damage repair proteins and radiosensitivity.

Eva-Leonne Göttgens
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Department of Radiation Oncology
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Nijmegen, The Netherlands



Resistance to radiotherapy and PD-L1 blockade is mediated by TIM-3 upregulation and regulatory T-Cell infiltration

Oweida A, Hararah M, Phan A, Binder D, Bhatia S, Lennon S, Bukkapatnam S, Van Court B, Uyanga N, Darragh L, Min Kim H, Raben D, Choon Tan A, Heasley L, Clambey E, Nemenoff R and Karam SD

Clin Cancer Res November 1 2018 (24) (21) 5368-5380;
DOI:10.1158/1078-0432.CCR-18-1038



NATASJA BALNEGER

Radiotherapy has the ability to change the immune landscape and thus make poorly immunogenic tumours sensitive to PD-L1 blockade. However, many tumours still evade the immune system after this combination treatment. In this paper Oweida *et al* investigate the mechanism behind this immune evasion. They show that the immune checkpoint receptor TIM-3 is upregulated on CD8 T cells and regulator T cells (Tregs) in tumours that received RT and anti-PD-L1. Combining radiotherapy with anti-PD-L1 and anti-TIM-3 did lead to significant inhibition of tumour growth in orthotopic models of murine head and neck squamous cell carcinoma. However, the effect did not last as relapsed tumours showed higher proportions of Tregs and less effector CD8 and CD4 T cells than early tumours. By combining Treg depletion with radiotherapy and the dual immune checkpoint blockade, Oweida *et al* were capable of restoring anti-tumour responses resulting in tumour regression and even immunological memory. Concluding, Oweida *et al* reveal the complexity of immune evasions by tumours and the important role of Tregs in this process.

Natasja Balneger
PhD student, ROI lab
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Nijmegen, The Netherlands



Radiotherapy induces responses of lung cancer to CTLA-4 blockade

Formenti SC, Rudqvist NP, Golden E, Cooper B, Wennerberg E, Lhuillier C, Vanpouille-Box C, Friedman K, Ferrari de Andrade L, Wucherpennig KW, Heguy A, Imai N, Gnjatic S, Emerson RO, Zhou XK, Zhang T, Chachoua A and Demaria S

Nature Medicine volume 24, pages 1845–1851 (2018)



LENNEKE
CORNELISSEN

Radiotherapy induces cancer cell damage, but importantly, radiation also causes exposure of tumour-specific antigens leading to higher visibility of the tumour for immune surveillance. The landscape of cancer treatment has drastically changed with the discovery of the immune checkpoint CTLA-4. Anti-CTLA-4 monoclonal antibodies are able to block the brakes of immune responses, allowing cytotoxic T cells to eliminate cancer cells. Enhancing tumour recognition with radiotherapy and releasing the brakes of immunity may unleash the immune system to eliminate cancer cells. As an example, Formenti *et al* have shown that radiotherapy and anti-CTLA-4 treatment induced systemic anti-tumour T cell responses in chemo-refractory metastatic non-small-cell lung cancer. Interestingly, a rapid *in vivo* expansion of CD8+ T cells specific for a neo-antigen encoded in a gene upregulated by radiotherapy has been observed in a responding patient. This supports the idea that radiotherapy induces exposure of immunogenic mutations to the immune system. Future research must demonstrate whether this example of the induction of a robust anti-tumour T cell response is unique or a common feature for the combination of radiotherapy and immunotherapy. In the meantime, the idea that radiotherapy may act as a sensitiser for immune checkpoint blockade suggests the need for more dedicated research to increase the effectiveness of combination therapy.

Lenneke Cornelissen
 Postdoctoral researcher, ROI lab
 Department of Radiation Oncology
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ATR kinase inhibitor AZD6738 potentiates CD8+ T cell-dependent anti-tumour activity following radiation

Vendetti FP, Karukonda P, Clump DA, Teo T, Lalonde R, Nugent K, Ballew M, Kiesel BF, Beumer JH, Sarkar SN, Conrads TP, O'Connor MJ, Ferris RL, Tran PT, Delgoffe GM, Bakkenist CJ.

J Clin Invest. 2018 Aug 31;128(9):3926-3940. doi: 10.1172/JCI96519.



PAUL SPAN

DNA damage induced by radiotherapy augments anti-tumour immune responses. Systemic effects of radiotherapy via these anti-tumour immune responses as manifested by so-called abscopal effects are rare, as several mechanisms counteract this effect, including, for example, PD(L)1 mediated immunosuppression. In this paper, the authors find that combining irradiation with ataxia-telangiectasia-mutated-and-Rad3-related kinase (ATR) inhibition increases CD8+ T cell-dependent anti-tumour activity by attenuating the immunosuppressive effects of irradiation (i.e. blocking the upregulation of PD-L1 and decreasing the number of immunosuppressive regulatory T-cells). ATR is crucial in the signalling of DNA damage repair and is known to be induced by hypoxia, thereby contributing to the radioresistance of hypoxic tumours. ATR kinase inhibition is known to augment (local) anti-tumour effects of DNA damaging treatments. However, this paper finds that combining ATR kinase inhibition with irradiation might indeed also have systemic effects. These data add to the growing number of possible combination treatments with radiotherapy leading to systemic and long-lasting anti-tumour effects.

Paul Span

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ESTRO SCHOOL





“We are launching a new academic entrepreneurship course as a pre-meeting workshop at ESTRO 38 in Milan, Italy”

NEW STAFF MEMBERS

Alessandra Nappa and Alexander MacDonald



We are pleased to welcome two new staff members to the ESTRO School: Alessandra Nappa and Alexander MacDonald. Both will be dedicated to the development of the School’s educational offer and its activities.

Our School is constantly striving to broaden its educational programme for the radiation oncology community and to provide training in all competencies necessary for good medical practice. As part of this mission, we are launching a new academic entrepreneurship course as a pre-meeting workshop at ESTRO 38 in Milan, Italy. This will be an excellent opportunity to learn more about collaborations between academia and industry, as well as technology transfer.

We hope that you will be interested in attending many of the courses being offered by the ESTRO School in 2019. In addition, and for those that cannot make the live courses, remember that you can register for the online FALCON delineation workshops.

Jesper Eriksen, Marie-Catherine Vozenin and Christine Verfaillie



JESPER ERIKSEN
Member and chair of the education council



MARIE-CATHERINE VOZENIN
Member of the education council



CHRISTINE VERFAILLIE
ESTRO Managing director education and science



FALCON CONTOURING WORKSHOPS



2019 ONLINE WORKSHOPS PROGRAMME

Mark your calendar ▶▶

FALCON workshop Mexican Radiation Oncology
Society Congress ▶▶

Mark your calendar

ESTRO members can benefit from a discount on the registration fee to attend an online workshop.

2019 ONLINE CONTOURING WORKSHOPS

Each online workshop includes two sessions

Breast Cancer	12 March 2019	26 March 2019
OAR - Head and Neck	2 April 2019	9 April 2019
Spine SBRT	10 April 2019	17 April 2019
Gynaecological Cancer - BT	21 May 2019	28 May 2019
Anal Cancer	25 September 2019	2 October 2019
OAR - Abdomen	8 October 2019	15 October 2019
Head and Neck Cancer	12 November 2019	19 November 2019
Liver SBRT	2 December 2019	9 December 2019

FALCON workshop at Mexican Radiation Oncology Society Congress

16 November 2018
Puerto Vallarta, Mexico



Some of the participants at the SOMERA congress

In November, the national congress of the Mexican Radiation Oncology Society (SOMERA) was held in Puerto Vallarta, Mexico. For the first time at the congress, ESTRO supported two on-site workshops in delineation. The FALCON team consisted of Elisabeth Arrojo, Arturo Navarro and Jesper Erikssen. The topics covered were stereotactic body radiation therapy (SBRT) in spine and rectal cancer.

The workshops featured great interaction between teachers and participants, which made it an excellent theoretical-practical experience. The workshop team was able to add to participants' theoretical knowledge as well as give them the chance to try things out in a very hands-on environment, with the teachers offering helpful tips. ▼



ELISABETH ARROJO



ARTURO NAVARRO



FALCON workshop in session

Among the attendees were radiation oncologists, physicists and therapists, who asked a range of questions focusing on their usual clinical practices and the resources available in their hospitals. This ensured the workshop provided updates based on the best clinical evidence, but was also individualised for participants and their situation.

In summary, we observed a really enthusiastic audience at the FALCON workshop. We particularly appreciated the open discussions about contouring among radiation oncologists. We believe that it was an interesting and valuable session. We look forward to repeating the experience at forthcoming SOMERA congresses.

*Elisabeth Arrojo
Arturo Navarro*



"The first ESTRO contouring workshop at the SOMERA congress was an excellent opportunity to get practical experience of rectal and spine SBRT using

FALCON. It was particularly helpful that the course was delivered in Spanish. The ESTRO workshop leaders were satisfied with the way the workshop went and hope to hold a similar delineation workshop at the next SOMERA congress."

Michelle Villavicencio



Grants available for attending international conference on medical education: AMEE 2019 ▶▶

24-28 August 2019 | Vienna, Austria

COURSE REPORTS

Positioning and immobilisation for radiotherapy ▶▶

Online sessions: From October to 22 November 2018
Practical weekend in Vienna, Austria: 3-4 November 2018

Accelerated partial breast irradiation ▶▶

11-14 November 2018 | Brussels, Belgium





Grants available for attending international conference on medical education: AMEE 2019

24-28 August 2019

Vienna, Austria

amee.org/conferences/amee-2019



The ESTRO School wants to support its faculty members to enhance their teaching skills. That is why, in 2019, we are again offering three grants to participate in this year's international conference on medical education in Vienna, Austria, in August – the AMEE conference. The deadline for applying for a grant is 31 May 2019 and we will select candidates based on their motivation and interest in medical education.

The three selected candidates will attend the conference on behalf of the ESTRO School. The aim is for these participants to then join the School's pedagogics programme, to help to build a 'think tank' culture, in which we continuously improve our education programme and offer.

The grant will cover the registration fee for the conference, travel to Basel and three nights' accommodation.

How to apply:

Please submit your CV and a short letter explaining your motivation for applying by email to: vvanegten@estro.org





COURSE REPORT

Positioning and immobilisation for radiotherapy

Online sessions:

From October to 22 November 2018

Practical weekend in Vienna, Austria:

3-4 November 2018

COURSE DIRECTOR:

Laura Mullaney



FILIPA SOUSA

I was drawn to this course due to the lack of guidelines on positioning and immobilisation in the literature. As radiation therapist (RTT) responsible for the implementation of image-guided radiation therapy (IGRT) protocols for all treatment sites in my department, the course was an opportunity to clarify some uncertainties that I had.

The course handled some important questions, such as how to evaluate positioning and immobilisation devices, and how they impact on target volume and organs at risk (OAR) delineation, on treatment planning, treatment verification and clinical outcomes.



Interactive sessions



Interactive sessions

The course took place over seven weeks, starting in October 2018. It was delivered using a blended learning approach (a combination of recorded online seminars, teleconferences and face-to-face teaching), which allowed me to organise my study time. The practical weekend and the live conferences were pleasantly animated, and it was great to discuss and share different points of view.

Theory and practice were well balanced. By the end of the course participants had an understanding of all the main subjects related to positioning and immobilisation, as well as some of the practical guidelines. It is important to mention that participants not only had the opportunity to attend both great lectures (during the practical weekend) and recorded online seminars, but were also able to speak with teachers and each other during the ▼



teleconferences and practical weekend. We also enjoyed a well-organised social dinner in Vienna, which helped us to get know each other.

I would definitely recommend this course to other RTTs, whether they are in charge of development in their department or not. Positioning and immobilisation is a crucial step in the radiotherapy process and a good understanding of this topic is essential to the success of any radiotherapy treatment. I also believe that this course makes a significant contribution to strengthening the RTT profession.

Finally, I would like to thank the course faculty for their enthusiasm and their engagement in sharing their knowledge and in invigorating the RTT profession. I would also like to give a special thanks to the project manager, Elena Giusti, for an exceptionally well-organised course.

Filipa Sousa
Research and development RTT
Institut Jules Bordet
Brussels, Belgium
filipa.rodrigues-sousa@bordet.be



In the radiotherapy department

Physicists take part in the: Pattern Of Practice for Adaptive and Real Time Radiation Therapy (POP-ART RT) survey

More details in the Physics Corner on page 58>



COURSE REPORT

Accelerated partial breast irradiation

11-14 November 2018
Brussels, Belgium

COURSE DIRECTOR:
Philip Poortmans



TOMÁS MERINO LARA

In November, I had the pleasure of attending the ESTRO teaching course on accelerated partial breast irradiation, a very topical area at the moment, which was held in the beautiful city of Brussels, Belgium. We arrived just in time for the city’s pre-Christmas preparations, with the cold temperatures and city lights setting the perfect stage for a great meeting.

The course gathered 52 participants from 22 countries across the world, including South Africa, Chile, Japan, Russia and Europe. The meeting involved the participation of six ESTRO faculty members and four guest speakers with cutting-edge knowledge and expert skills covering every area of this interesting topic.

Some of the highlights of this meeting included an overview of imaging and pathology, an interesting lecture on breast reconstructing surgery given by Petrousjka van den Tol, recent advances in brachytherapy, and a review of external beam results by Birgitte Offersen. Finally, as a concluding activity, on day four a panel of experts reviewed controversial topics related to treatment toxicities. The participants had ample time to take part in the discussions that continued into the breaks and the social evening.

Overall, the course was a great opportunity to learn about the state-of-the-art in accelerated partial breast irradiation, and a perfect chance to meet old friends and to make new ones. Unfortunately, time goes by so quickly and before I knew it, I was flying back home after four intense days. But not before trying some Belgian beers and chocolates, both the world’s very best.

I thank the course director, the faculty members and the ever-present ESTRO staff, as well as my new friends for an enjoyable four days and a great learning experience.

Tomás Merino Lara, MD
Radiation oncologist
Pontificia Universidad Católica de Chile Cáncer Center, Chile
[*tomasmerinolara@gmail.com*](mailto:tomasmerinolara@gmail.com)



ESTRO School of Radiotherapy and Oncology

WWW.ESTRO.ORG

POSTGRADUATE COURSES IN EUROPE

Image-Guided Radiotherapy in Clinical Practice

17-21 February 2019 | Porto, Portugal

Basic Clinical Radiobiology

3-7 March 2019 | Brussels, Belgium

Comprehensive and Practical Brachytherapy

3-7 March 2019 | Athens, Greece

Particle Therapy

18-22 March 2019 | Groningen, The Netherlands

Lower GI – Technical and Clinical Challenges for Radiation Oncologists

20-22 March 2019 | Amsterdam, The Netherlands

Upper GI – Technical and Clinical Challenges for Radiation Oncologists

23-26 March 2019 | Amsterdam, The Netherlands

Foundation of Leadership in Radiation Oncology

26 April 2019 | Milan, Italy

ESTRO/ESMIT course on Molecular Imaging and Radiation Oncology

6-9 May 2019 | Florence, Italy

Advanced Skills in Modern Radiotherapy

19-23 May 2019 | Brussels, Belgium

Multidisciplinary Management of Prostate Cancer

19-23 May 2019 | Pisa, Italy

Dose Modelling and Verification for External Beam Radiotherapy

19-23 May 2019 | Lisbon, Portugal

Target Volume Determination – From Imaging to Margins

2-5 June 2019 | Athens, Greece

IMRT and Other Highly Conformal Techniques in Practice

2-6 June 2019 | Budapest, Hungary

Brachytherapy for Prostate Cancer

13-15 June 2019 | Prague, Czech Republic

Evidence Based Radiation Oncology

24-29 June 2019 | Montpellier, France

Clinical Practice and Implementation of Image-Guided Stereotactic Body Radiotherapy

1-5 September 2019 | Florence, Italy

Physics for Modern Radiotherapy

A joint course for clinicians and physicists

8-12 September 2019 | Riga, Latvia

Advanced Treatment Planning

22-26 September 2019 | Budapest, Hungary

Imaging for Physicists

29 September - 3 October 2019 | Manchester, UK

Image-Guided Radiotherapy and Chemotherapy in Gynaecological Cancer: Focus on MRI Based Adaptive Brachytherapy

12-16 October 2019 | Cluj, Romania

Comprehensive Quality Management in Radiotherapy – Quality Assessment and Improvement

13-16 October 2019 | Dublin, Ireland

Best Practice in Radiation Oncology

Train the RTT (Radiation Therapists) Trainers - Part II

14-16 October 2019 | Vienna, Austria

Positioning and Immobilisation for Radiation Therapy

19-20 October 2019 | Brussels, Belgium

Multidisciplinary Management of Breast Cancer

27-30 October 2019 | Budapest, Hungary

Research Course in Radiation Oncology

*How to develop research/validation programmes when
implementing new technology?*

Edition 1: MRI Linac

3-6 November 2019 | Madrid, Spain

NEW

Research Course in Radiotherapy Physics

3-6 November 2019 | Madrid, Spain

ESTRO/ESOR Multidisciplinary Approach of Cancer Imaging

4-5 November 2019 | Amsterdam, The Netherlands

Multidisciplinary Management of Non-Melanoma Skin Cancer

7-9 November 2019 | Brussels, Belgium

Palliative Care and Radiotherapy

*A course on prognosis, symptom control, re-irradiation,
oligometastases*

26-28 November 2019 | Brussels, Belgium

Paediatric Radiotherapy

1-3 December 2019 | Utrecht, The Netherlands

Multidisciplinary Management of Brain Tumours

1-3 December 2019 | Brussels, Belgium

2019



POSTGRADUATE COURSES OUTSIDE EUROPE

3D Radiotherapy with a Special Emphasis on Implementation of MRI/CT Based Brachytherapy in Cervical Cancer

14-17 March 2019 | Rishikesh, India

Palliative Care and Radiotherapy

*A course on prognosis, symptom control, re-irradiation,
oligometastases*

26-28 March 2019 | Manila, Philippines

Combined Drug-Radiation Treatment: Biological Basis, Current Applications and Perspectives

7-9 June 2019 | Seoul, South Korea

Multidisciplinary Management of Head and Neck Oncology

28-31 October 2019 | Mexico City, Mexico

Advanced Technologies

3-6 November 2019 | Shenzhen, China

Advanced Technologies

India | Date and venue to be announced

PRE-MEETING COURSES

Eight Pre-Meeting Courses at ESTRO 38

26 April 2019 | Milan, Italy

UNDERGRADUATE COURSES

Medical Science Summer School Oncology for Medical Students

15-27 July 2019 | Vienna, Austria

ESO-ESSO-ESTRO Multidisciplinary Course in Oncology for Medical Students

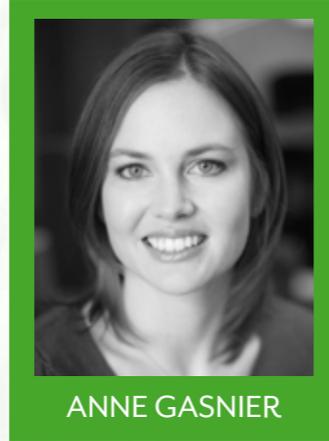
26 August - 6 September 2019 | Turin, Italy



YOUNG ESTRO



“Working in a strongly regulated environment increases the difficulty of moving countries, but learning from different practices is a real benefit”



ANNE GASNIER

Welcome to the Young Corner. I would like to thank Kathrine and Pierfrancesco for this opportunity to be guest editor for this issue, and to all those who contributed to the Corner.

Having recently moved from England to France, I have dedicated the first article to the mobility of radiation oncology professionals in Europe. Working in a strongly regulated environment increases the difficulty of moving countries, but learning from different practices is a real benefit. Three former colleagues – Rita Simões (a radiation therapist),

Laurent Basson (a radiation oncologist) and Petra Trnkova (a medical physicist) – kindly agreed to share their experiences. I hope this will encourage you to visit other European departments and share best practices.

This Corner also features a report from Mateusz Spalek who attended the Young Scientific Forum in Poznan, Poland, in November 2018. This forum is aimed at radiation oncologists, medical physicists and radiobiologists to help them promote their work and meet fellow young scientists. I would like to congratulate Mateusz on receiving an award for his work on preoperative hypofractionated radiotherapy of soft tissue sarcomas.

Finally, you can learn about the hot topic of radiomics by reading the report from Elizabeth Forde, who received a mobility grant to visit the San Raffaele Scientific Institute, in Milan, Italy. She goes through the process and challenges of applying this quantitative image analysis for the assessment of radiation induced normal tissue damage. If you're interested in this topic, please join us during ESTRO 38 at the session on 'Predictive models of toxicity and big data' chaired by Claudio Fiorino.

We also hope to see you at the Young Track at ESTRO 38, which will include scientific and career-related content dedicated to young ESTRO members – don't forget to look at the programme at the end of this newsletter.

*Anne Gasnier,
Young ESTRO member*



KATHRINE RØE
REDALEN



PIERFRANCESCO
FRANCO

MOBILITY IN EUROPE

The experiences of three young oncology professionals

Rita Simões, radiation therapist ▶▶

Laurent Basson, radiation oncologist ▶▶

Petra Trnkova, medical physicist ▶▶

The experiences of two ESTRO Mobility Grant Awardees

Radiomics assessment of radiation-induced parotid gland changes
Elizabeth Forde ▶▶

High precision radiotherapy in primary and metastatic lung tumours
Vikas Kothavade ▶▶

The experiences of three young oncology professionals



Rita Simões, radiation therapist

Thank you to the editors of the Young Corner for inviting me to share my experience of working across Europe. In this

piece, I reflect on some of the differences that I have found working in Portugal, where I started my career as a radiation therapist, and the UK, where I am based now.

At the start of my career I worked for almost five years in the Hospital de Santa Maria, Lisbon, in both pre-treatment and treatment areas. In late 2012, I moved to the UK and started working at Mount Vernon Hospital, London, in dosimetry planning. In April 2015, I took on a new role at the same hospital, working in radiotherapy quality assurance (RT QA), as part of the UK Radiotherapy Trials Quality Assurance (RTTQA) Group. So why did I decide to swap the beautiful blue skies of Lisbon for London in the first place? Back in 2011, I completed my MSc and wanted to become more involved in research, clinical trials and the development of new

techniques. Unfortunately, at the time, these were not high priority for the Portuguese government. There was an economic recession in Portugal and the health and science sectors suffered deep financial constraints. This made opportunities for developing radiotherapy-related science, including clinical trials, very rare. Therefore, I decided to follow my ambitions by moving to a country where I could develop my career in this direction and also experience working and living abroad. As we say in Portugal, my move “killed two rabbits in a single stroke”, or as the British would say, “killed two birds with one stone”! In moving to a country with a reputation for radiotherapy research and technical excellence I expected to have numerous opportunities for learning. What surprised me was that my own experience in Lisbon was equally valuable in enabling me to contribute to the development of new ideas and ways of working. One of the key lessons I learnt was that, although there are differences in working between countries, you can always make a positive contribution. Let me expand. It came as a surprise to me to find out that, back in 2012, most UK centres still relied on paper documentation, whereas most centres in Portugal had already moved to paperless, ▼

computer-based solutions. This early move from paper to computer stems, perhaps, from very developed IT teams and highly skilled engineers who promoted this transition as a priority. Portugal is home to many companies producing IT health solutions, which have been widely implemented in a coordinated way across the country's hospitals. This experience of working in a paperless department, put me in an ideal position to support the implementation of a move to a paperless department in the UK.

Another big difference in practice was the implementation of technology. The UK is a frontrunner in technology implementation and also has a strong tradition in radiotherapy technique development through the clinical trials arena. In contrast, Portugal saw fewer clinical trials in radiotherapy, and home-grown research was the notable exception rather than the rule. Finding funding opportunities in this field was challenging and innovative treatments were adopted after first being researched in other countries. Nevertheless, most Portuguese centres used advanced radiotherapy techniques, which is a credit to the highly skilled and qualified professionals who use the available resources to their maximum potential, providing patients with high-quality treatment.

Portuguese departments are fewer and generally smaller than in the UK, especially compared to the larger centres in UK cities. Management structures are also different. Working in smaller groups means that local communication and decision-making is easier in Portugal, as everybody gets to know each other. Working in larger departments, with a high staff turnover, sometimes involves more bureaucracy to maintain uniform procedures.

My subsequent work in the RTTQA group has made me very aware of the complexity of setting up multicentre clinical trials and has provided me with an insight into the need to standardise processes and procedures across centres in order to ensure trials report accurately, and to ensure that new technologies can be implemented into routine practice.

I feel that my experience of employment in two different countries has given me the opportunity to develop a curiosity and interest around different ways of working and has also broadened my knowledge, both clinical and scientific, allowing me to grow professionally as a radiation therapist.

I think that if you have the opportunity to do so, you should try a leap over borders. It will give you experience and a new perspective and is a great way of making new friends in the radiotherapy family.



“WOMEN IN MEDICAL PHYSICS - MEET AND GREET”

Sunday 28 April
8:00-9:00 | Open space area of Exhibition

ESTRO 38, Milan



Dr Laurent Basson, radiation oncologist

I was invited by Anne Gasnier, guest editor, to share my experience as a French radiation oncologist working in

the UK. I undertook medical studies at the University of Lille, France, and most of my training in radiation oncology at the Oscar Lambret Comprehensive Cancer Centre, Lille.

As a clinical resident in France, you can do six-months clinical practice in another region, known as an 'InterCHU'. I wanted to spend the last semester of my training overseas. I discussed this with Professor Lartigau and he recommended the Royal Marsden Hospital in London, UK. I contacted Dr van As, radiation oncologist and medical director of the Royal Marsden, and he welcomed the idea. And so in 2017, I spent the last semester of my training at the Royal Marsden Hospital.

As this programme is funded by the university where you study, the first step was to submit an application to the University of Lille



Laurent with the welcoming radiotherapy team at the Royal Marsden Hospital

describing my project. My project was focused on prostatic cancer and the Royal Marsden is a pioneer for hypofractionated radiotherapy in prostatic cancer, especially through the CHHIP and PACE trials, the results of the latter still pending. The second step was administrative, filling and sending different documents to the Royal Marsden Hospital. To take full advantage of this experience, I wanted to work as a local resident, and not just be an observer. To do this, I needed to register with the General Medical Council (GMC) in the UK. As part of various EU agreements, I simply needed to provide evidence of my studies

to have my French medical degree recognised as an equivalent to a UK degree. In order to get the license to practice, I also needed to take an International English Language Testing System (IELTS) exam to demonstrate that I had a good level in English. It may also be possible to do this through your employer. At the Royal Marsden, I was welcomed warmly. I saw patients on my own, undertook contouring, and participated in brachytherapy procedures and multidisciplinary team meetings. Visiting different hospitals in your own country enables you to discover new machines, treatment planning systems, techniques, and ▼



A visit to Twickenham to watch some rugby

clinical practices. These differences are even more pronounced in a different country.

There are, for example, a number of differences in training programmes in France and the UK. In the UK, you have to pass regular exams, which are difficult and can be stressful. In France, you validate your residency through a thesis, which, until recently, enabled you to graduate. To become a specialist in the UK, you need 13 to 14 years' experience compared to 11 years in France. In the UK, more experienced senior residents are able to validate from A to Z some radiotherapy treatments, such as palliative treatments, which is not the case in

France. There are a number of other features that are specific to the UK, such as organised telephone consultations, specialist nurses performing follow up visits, therapeutic radiographers performing on-treatment visits, and even inserting gold markers in the prostate, which you would not see in France.

The organisation of healthcare systems is also quite different in the UK. Everyone in France is partly or totally covered by 'Sécurité Sociale' (national insurance), depending on your financial situation and type of disease. You can select an additional insurance 'complémentaire santé' to complete your cover. Whatever the level of financial coverage, everyone has equal access to care. Healthcare in private clinics might be more expensive in other specialities, but in private radiation oncology centres it is generally the same. In the UK, everyone is covered by the NHS, but some people might choose to take out private health insurance, which can offer quicker access to specialists. Also, the NHS only funds radiotherapy in precise indications and fractionation, and the radiation oncologist is not supposed to perform any treatment outside the validated indications. However, the radiation oncologist is free to do so in private practice, but the treatment is not always funded

by health insurance. In France, the radiation oncologist is free to perform any treatment or fractionation they consider as scientifically indicated. Each system has its pros and cons.

I was impressed by the organisation and support around research activities in the UK. Research nurse specialists were always available when we were doing consultations. Before seeing patients, they gave us useful information, for example, about whether a patient could be included in a trial. They then briefed the patient about the study and collected their consent. This system clearly supports the inclusion of patients in clinical trials.

The Royal Marsden is divided across two sites, one in Chelsea in central London and one in Sutton in south London. I did my entire placement at the Chelsea site, a very nice part of London. I had to find myself accommodation and London is expensive. However, London was quite convenient for me, because there is a direct Eurostar train from London to Lille, which only takes 1 hour and 20 minutes, so I could go back home regularly if I wanted to.

Of course, my visit was also an opportunity to improve my English skills, to meet new ▼

people, to make new friends and discover a new culture. I spent some time enjoying being a tourist in London, such a beautiful city, with so many places to visit and also visited a few places outside the city. As a sports fan, I really enjoyed watching some live football, rugby, tennis and athletics.

Living and practicing abroad was a great experience in so many ways, and I could speak about it for hours. If you have the opportunity, I would recommend it to anyone.

I would like to thank Professor Lartigau for suggesting the Royal Marsden and helping me with my first contacts, Professor Gosset and Dr Sobanski at the University of Lille for accepting this project, and finally Dr van As and all the Royal Marsden radiation oncology department for welcoming me. It was one of the best times of my life.



Dr Petra Trnkova, medical physicist

Moving jobs as a clinical medical physicist within Europe is not as simple as it could be. In most countries, a medical

physicist is a healthcare professional. Therefore, you need recognition of your medical physics expertise in the country you intend to practice. The requirements of each country differ significantly and transition from one country to another is not always easy.

The issue starts at university level. In some countries, a master's in physics is an essential pre-condition to enter a medical physicist training programme, whereas in others, an equivalent master's in biomedical engineering is sufficient. The training programme itself has different forms. In some places you must complete postgraduate studies in medical physics, plus several years of clinical experience, to become a certified medical physicist. Elsewhere, the postgraduate educational programme is replaced by a personalised residency. Some systems place a lot of emphasis

on being highly specialised in one of the fields of medical physics (radiotherapy, nuclear medicine, diagnostics or audiology), others require a general knowledge of the whole field. Some programmes are concluded with a final exam, a second master's thesis or both, while for others completing the programme is sufficient.

All these national approaches have one thing in common. It takes several years – the exact time varies from country to country – to become a fully certified medical physicist. You can imagine then that if one national programme is not recognised by another country, it's possible to be in a permanent state of training to become a medical physicist, especially if you are moving countries regularly.

But I've always been drawn to new challenges, which is why I've worked as a clinical medical physicist in several countries across Europe: the Czech Republic, Austria, Switzerland and The Netherlands. At times I felt like all I was doing was working to be recognised as a medical physicist. Without going into the details, it always took years to receive certification in a new country and it was never a straight-forward process. I had to invest a lot of time on administration, translating all ▼

the documents, and bothering my previous employers by asking for written confirmation of my responsibilities and tasks. I never had to repeat a training / residency programme in a new country, but I always had to do something extra: courses, exams and even an adaptation internship (after many years working in the field). But even though the process was complicated, it was worth it. I have had exciting jobs and been involved in very interesting projects. I have seen lots of different medical physicist roles, and it has helped me to take my career in the direction I would like.

Moving for work within Europe takes lots of effort and personal dedication. In addition, your ability to receive recognition in a country is often a limiting factor in the recruitment process. A unified system of medical physics certification within the Europe would make mobility much easier.

There is already an initiative to create unified medical physics training in radiotherapy within Europe, and the European Federation of Organisations for Medical Physics (EFOMP) together with ESTRO agreed the syllabi for training and education. The European Examination Board (EEB) will

award a European Diploma of Medical Physics (EDMP) and European Attestation Certificate for Medical Physics Expertise (EACMPE). Currently, these diplomas will not replace any national certificates. However, in the future it is hoped there will be a common European qualification for medical physicists, which will help to standardise training and expertise across Europe.



New series on PhD research in the Physics Corner

Have you just completed or are you about to complete an interesting PhD thesis?

Then please share it with the ESTRO physics community by contacting Christian at christian.richter@oncoray.de for more details. If your report is accepted by the editors of the Physics Corner, it will be published in a forthcoming issue of the newsletter.

The experiences of two ESTRO Mobility Grant Awardees

Radiomics assessment of radiation-induced parotid gland changes

Elizabeth Forde

HOST INSTITUTE:

Department of Medical Physics, San Raffaele Scientific Institute, Milan, Italy
6-9 November 2018



ELIZABETH FORDE

It was while attending the ESTRO Physics Research Masterclass in 2017 that I first met Claudio Fiorino. We shared an interest in the application of quantitative imaging analysis for the assessment of radiation-induced normal tissue damage. One of the aims of the Masterclass was to provide a platform that encourages future collaboration and mentorship between faculty members and participants. Based on this, and the previous work by the researchers at San Raffaele Scientific Institute, I felt a visit to their site would be hugely beneficial to develop my research goals. I was lucky to receive an ESTRO mobility grant, which funds visits that will result in a transfer of critical skills relating to the application of advanced technologies.

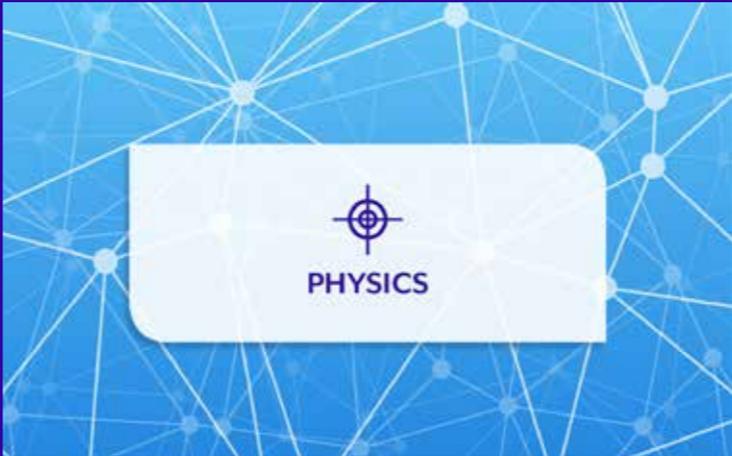
On the anniversary of Marie Curie’s birth in November, I presented myself to Claudio and his team at San Raffaele Scientific Institute, where I was introduced to Martina Mori (#womenwhocurie), a medical physicist researching a range of novel applications of radiomics. Over the coming days I worked closely with Claudio and colleagues to examine methodically the process and challenges relating to radiomics, the details of which are listed below.

- 1. Image acquisition:** We discussed the importance of image quality to ensure the radiomics “chain” is not compromised. Using MIM software I was shown how to correct for inter-scanner variability to ensure some level of image standardisation prior to analysis.
- 2. Region of interest segmentation:** We discussed the impact inter-observer contouring variability can have on the robustness of radiomics features extracted. Always generous with her time, Martina went through in detail her previous research examining this issue.
- 3. Feature extraction:** Having no previous practical experience with quantitative imaging software, I was grateful to be shown first-hand the Chang Gung Image Texture Analysis (CGITA) interface and exactly how data are imported, and features extracted and then exported for subsequent analysis.
- 4. Feature selection:** Correct feature selection and validation is critical to the radiomics process. Again, through presentation of previous work in this field, we examined the process of identifying the most robust and clinically meaningful features for analysis. ▼

5. Data analysis, including correlation with clinical information and prediction of outcomes: Finally, we discussed the important link of quantitative imaging data with clinical data. Specifically, in relation to normal tissue damage, we discussed the importance of assessment of side effects during radiotherapy and standardisation in toxicity scoring/reporting.

Fuelled by Italian espresso and a shared interest in quantitative imaging the time spent together was both enjoyable and scientifically beneficial. As a result of the generosity and scientific knowledge of the staff at San Raffaele, I can definitively say both my primary and secondary aims were met. This visit was only made possible with the funding received from the ESTRO mobility grant, for which I am very grateful.

*Ms Elizabeth Forde
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Physicists take part in the: Pattern Of Practice for Adaptive and Real Time Radiation Therapy (POP-ART RT) survey

More details in the Physics Corner on page 58>



**ESTRO
PHYSICS
workshop**

25-26 October 2019
Budapest, Hungary

The experiences of two ESTRO Mobility Grant Awardees

High precision radiotherapy in primary and metastatic lung tumours

Vikas Kothavade

HOST INSTITUTE:

Centre: VU university medical centre, Amsterdam, The Netherlands

10 to 29 December 2018



VIKAS KOTHAVADE

VU university medical centre (VUmc) in Amsterdam treats more than 300 patients a year with high-precision radiotherapy techniques such as stereotactic body radiotherapy (SBRT). This visit to the centre was essential to setting up the standard protocol in my centre in Jupiter Hospital, Pune, India, which has just initiated an SBRT programme.

As part of my visit, I learned to conduct SBRT at extra-cranial sites, including immobilisation procedures, CT simulations, delineation of targets, plan evaluations, treatment set-up and image verification during treatment. I was able to discuss with VUmc clinicians issues around the indications for SBRT, plan evaluations, toxicity, follow-up schedules and imaging protocols. These discussions will help to increase and improve the use of SBRT in my clinical practice. We also discussed alternatives to 4D-CT, such as slow CT scans, scans in the extreme phase of breathing (end inspiration, end expiration), free breathing, use of 4D cone beam CT and fluoroscopy for internal target volume generation. I learned about using gating in mediastinal and abdominal tumours other than breast and lung.

We assume SBRT requires rigid immobilisation, but VUmc’s approach is to use relaxed,

comfortable immobilisation, with most patients treated using a wing board with knee support. Faster treatment delivery, use of intrafraction cone beam CT, and faster IGRT correction help to minimise errors.

I observed utilisation of MRdian for MR-guided adaptive radiotherapy using online contouring, and re-planning considering daily anatomy.

VUmc has incorporated patient workflow within the Eclipse planning system, which means that the department is paperless and ensures easy communication among physicians, planners, physicists and technologists. Treatment site-specific protocols with planning objectives are also incorporated within the Eclipse system, helping staff to start and then evaluate the plan easily. In head and neck cancers, automated plans are generated using a planning database with 100 patients.

Along with a physicist, I spent time planning using MRdian, Eclipse, and iPlan by Brainlab. This helped me to understand differences in the planning processes, and will help me to produce better planning protocols at my centre. ▼

Each day started with a morning report, in which all new patients are discussed before starting their treatment, which gives excellent exposure to a wide range of diagnosis and radiation plans. I attended the weekly lung tumour board meeting to understand the treatment algorithm and approach to each case.

This visit definitely improved my understanding of stereotactic radiotherapy in lung and other sites, which will help me to create in-house protocols at my centre.

Finally, I am very grateful to the ESTRO committee for giving me this opportunity and Professor Suresh Senan, and all the VUmc team for their support and hospitality.

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PHYSICS ASSEMBLY

Monday 29 April
13:30-14:30 | Room Brown 1

ESTRO 38, Milan



A report from the Young Scientific Forum 2018 in Poznan – the perspective of a participant and prize winner



MATEUSZ SPALEK

What makes us scientists? Is that term reserved only for people who have prestigious professional titles or who have made remarkable discoveries? No. I would argue that everyone who tries to use their curiosity to empirically solve a problem or answer a question is a scientist. I agree with Richard Feynman, the American theoretical physicist, who said: “I don't feel frightened by not knowing things, I think it's much more interesting.”

Even young radiation oncology scientists have opportunities to present their ideas, concepts and results to other professionals. On 26 November 2018 in Poznan, at the Greater Poland Cancer Centre, the Young Scientists' Forum (YSF) took place, and I attended for the third time.

The aim of the conference is to promote the achievements of young scientists, to help with their professional development, and to create a strong platform to exchange professional experiences. The YSF is aimed at radiation oncologists, medical physicists and radiobiologists aged 35 or younger. Abstracts were evaluated by an international jury consisting of leading experts in radiotherapy, radiobiology, and medical physics:

- Dr Joanna Kaźmierska, scientific chair (Poland)
- Professor Julian Malicki, honorary chair (Poland)
- Professor Ursula Nestle (Germany)
- Professor Andreas Osztavics (Austria)

- Professor Uwe Oelfke (UK)
- Professor Vincenzo Valentini (Italy)
- Professor Andrzej Wójcik (Sweden).

The accepted abstracts were classified into two categories – oral presentation or poster. Oral presentations consisted of a ten-minute presentation followed by a ten-minute discussion. Posters had to be presented in front of the jury in five minutes.

My impressions of the YSF

I wrote a similar report a few years ago when I participated in YSF for the first time – from the perspective of three people, a participant, a member of the audience, and a jury member. This time I can add a fourth viewpoint: the perspective of a prize winner.

The audience perspective

YSF 2018 was a really interdisciplinary conference, with extraordinary studies, and very interesting and diversified topics. As an audience member, I noticed a lot of familiar faces from previous editions, but also many new young scientists who wanted to present results from their studies. Luckily, my presentation was at the very beginning, so I was able to relax after that and focus on listening to other people. The discussions were intense, with a high educational value. Everything was well organised and there were no delays in the programme. ▼

The participant perspective

I remember my first time as an oral presenter at YSF – I was extremely stressed. This time was much better, but not without nerves. My advice for overcoming emotions and stress, is to take lots of exercise and practice presenting as much as you can. This builds up your self-confidence. The most valuable part of any presentation is always the discussion with the jury of well-known radiation oncology experts. The discussion after my presentation was valuable; I got lots of new ideas to improve my study, and even ideas for new ones. Emotions were running high when it came to results. And... I won the first prize. Wow!

The winner's perspective

It is very hard to describe the flow of positive emotions. For sure I was, and still am, very happy! It gave me the confidence to conduct new projects and it destroyed a myth (in my head) that in Poland it is impossible to do science. I received congratulations from jurors and colleagues, although they were not able to participate in the YSF. Sometimes this study was very hard, but I feel satisfied now. And I know that I would like to pursue it in the future.

The jurors' perspective

Jurors have a very demanding task – to judge a wide range of valuable studies, but also to ask questions and to have discussions with participants. Sometimes the discussion was very intense, and it went over the time limit.

The most important part of the juror's work is to give notes and select winners. I was not a juror this year, but I know how hard it is to select winners. This time the task was slightly easier, because the organising committee provided additional book prizes.

The major awards in 2018 were:

- First place – participation in a chosen European ESTRO 2019 course (fee, travel and accommodation)
- Second place – participation in a chosen European oncology conference (fee, travel and accommodation)
- Third place – annual subscription to the journal *Reports of Practical Oncology and Radiotherapy*.

And the list of winners in 2018:

- First place: Mateusz Spalek for 'Preoperative hypofractionated radiotherapy with sequential chemotherapy in primary marginally unresectable or marginally resectable high grade soft tissue sarcomas of extremities or trunk wall: an interim analysis of prospective phase II clinical trial' (Centrum Onkologii Warsaw, Poland)
- Second place: Igor Piotrowski for 'Surgical wound fluids collected from breast cancer patients increase migration of cancer cells; however, this effect is impaired by intraoperative radiotherapy through radiation-induced bystander effect' (Wielkopolskie Centrum Onkologii Poznań, Poland)

- Third place: Theresa Suckert for 'Development of a preclinical model to investigate radiation effects after proton brain irradiation' (OncoRay Dresden, Germany)
- Best poster: Agnieszka Sobocka for 'Micro RNA hsa-miR-6510-3p: potential tumour suppressor in head and neck cancer' (Wielkopolskie Centrum Onkologii Poznań, Poland).

Again, I would like to congratulate the chair, Dr Joanna Kazimierska, the honorary chair, Professor Julian Malicki, and the whole YSF organising committee for the excellent conference. They have dedicated their time to create opportunities for young radiation oncology professionals, who may become scientific leaders in their sub-disciplines. A conference like this shows that everyone can be a scientist.

On behalf of the Young ESTRO committee, I would like to thank all the young scientists for coming and would encourage more young radiation oncology professionals to participate in events like this. And a few final words. I still have five more years to participate in forthcoming YSFs. I cannot be complacent. I hope to see you in Poznań!

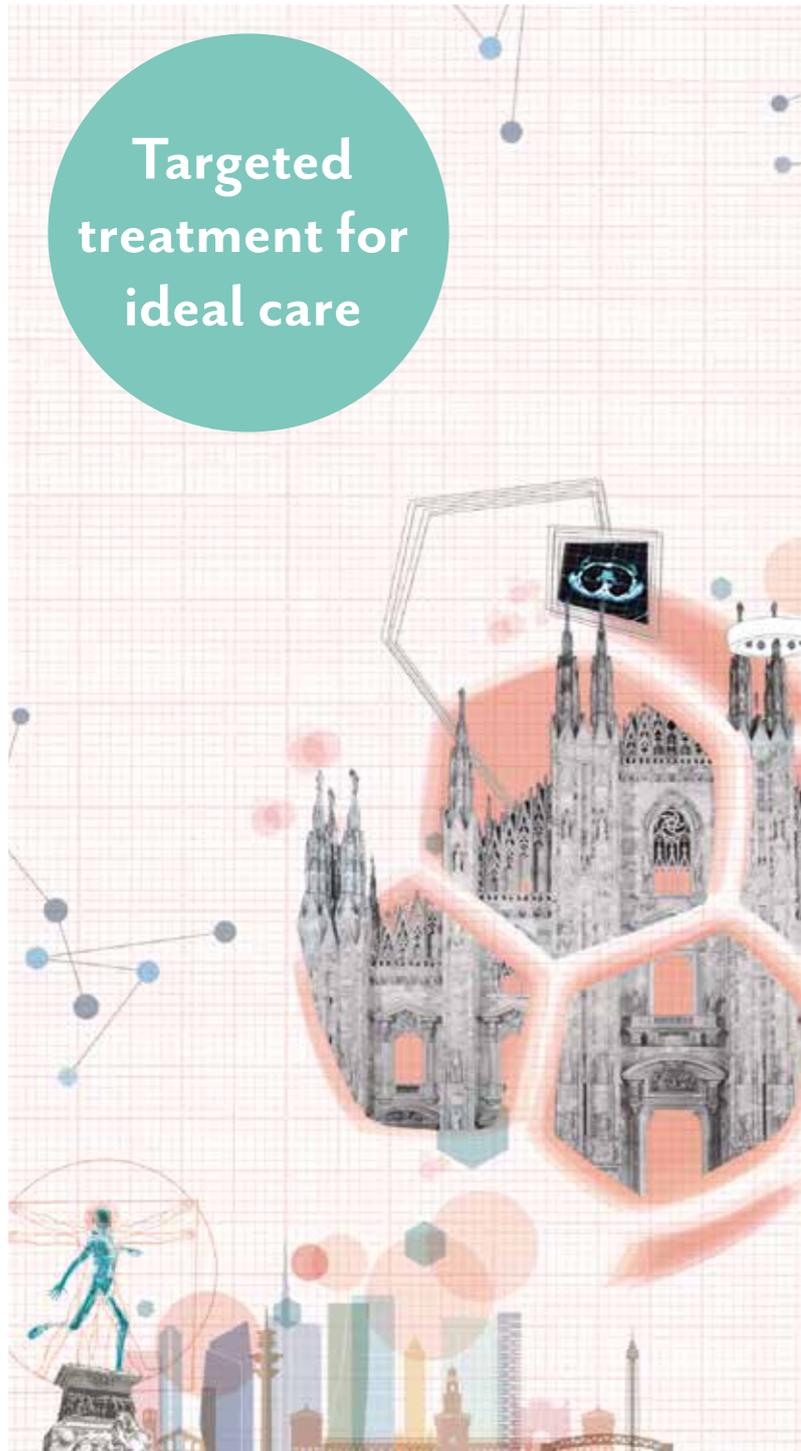
*Mateusz Spalek,
Maria Skłodowska-Curie Memorial Cancer Centre
Warsaw, Poland*

Young track at ESTRO 38

Sunday 28 April 2019
Milan, Italy

Martin-Immanuel Bittner and Cyrus Chargari
Chairs of the Young track at ESTRO 38

8:00-8:40	<p>TEACHING LECTURE</p> <p>Precision medicine and systems biology - transforming cancer research in the 21st century</p> <p><i>Chair: M-I Bittner (Germany)</i></p> <p><i>Speaker: W. Kolch (Ireland)</i></p>
8:45-10:00	<p>SYMPOSIUM</p> <p>Combining research and (clinical/ professional) training/ practice</p> <p><i>Chair: C. Chargari (France)</i></p> <p><i>Co-chair: G. Reggiori (Italy)</i></p> <p>Taking time off for full-time research - is it worth it? <i>A. Levy (France)</i></p> <p>Why do we need to be trained in statistics? Need and pitfalls. <i>A. Escande (France)</i></p> <p>Research and training in medical physics. <i>S. Petit (The Netherlands)</i></p> <p>Clinical vs lab research for clinicians Combining research and (clinical/professional) training /practice. <i>D Milanovic (UK)</i></p> <p>Lessons learnt from a young head of department. <i>R. Baumann (Germany)</i></p>
10:00-11:45	<p>COFFEE BREAK & SPEED DATING</p> <p><i>Chair: M-I Bittner (UK) and C. Chargari (France)</i></p>
13:00-14:30	<p>YOUNG LUNCH SYMPOSIUM</p> <p>How to prevent burnout?</p> <p><i>Chair: J-E Bibault (France)</i></p> <p><i>Co-chair: J Bertholet (UK)</i></p> <p>Perspectives on burnout in the medical professions. <i>P Franco (Italy)</i></p> <p>E38-1299 The PRO BONO survey (PROject on Burn-Out in RadiatioN Oncology). <i>P Franco (Italy)</i></p> <p>▼</p>



13:00-14:30

Science slam:

Report back from ESTRO mobility grants clinical: SRS & SBRT in the management of oligometastatic disease. *Zumbadze (Georgia)*

Modelling Head and Neck Radiotherapy outcomes using radiomics biomarkers. *P Kalendralis (The Netherlands)*

To breathe or not to breathe. ESTRO Mobility Grant report. *S Prcic (Slovenia)*

14:30-15:45

SYMPOSIUM

Stronger together - news and projects in the young national societies

(each talk to contain 3 ideas for concrete projects with yESTRO & respective young national societies)

Chair: N Ebert (Germany)

Co-chair: O Kaidar-Person (Israel)

Perspective of an established young society: the Spanish Young Society.

V Morillo (Spain)

An emerging young society: Young Romanian Radiotherapists and Oncologists Group (YRROG). *M Zerbea (Romania)*

Creating a new young radiation oncology society - the case of Poland Group.

M Spalek (Poland)

Working together across borders: YROG. *C Ostheimer (Germany)*

Panel discussion - Speakers and session chairs

15:45-17:00

The Stage

QUIZ AND YOUNG NETWORKING COCKTAIL

Chair: L. Dubois (The Netherlands)



HEALTH ECONOMICS

Radiotherapy in Rwanda

Although radiotherapy has been estimated to lead to a cure in 40% of patients [1], few readers would have been surprised when the International Atomic Energy Agency reported in 2015 that 28 African countries lacked a single radiotherapy machine [2]. More than any other essential component of cancer care delivery, radiotherapy faces unique implementation challenges related to the cost of machine purchase, the technical expertise in radiation oncologists, therapists, physicists, radiation nurses and maintenance. These challenges lead to radiotherapy often being viewed as a treatment modality that is too expensive and too complex, resulting in its frequent absence in cancer centres in low- and middle-income settings.

Rwanda is one of the 28 African countries and the challenges faced there are well described by Hanappe *et al* [3] in their retrospective study of a selected group of patients diagnosed with cervical, head and neck, or rectal cancer attending the Butaro Cancer Centre of Excellence (BCCOE), which is located close to the country's northern border with Uganda and 90km away from the capital Kigali. Originally presented at the 2016 World Cancer Congress in Paris and published in the October 2018 issue of *Journal of Global Oncology*, the authors report a novel implementation strategy: a protocol-driven, out-of-country referral programme for providing life-saving radiotherapy services for cancer patients living mainly in an under-resourced rural setting.

Between 2012 and 2015, 580 Kenyan patients diagnosed with these malignancies were potential candidates for radiation therapy. Of these, 208

patients (36%) were referred for radiotherapy treatment at the Uganda Cancer Institute (UCI) Mulago in neighbouring Uganda. Ten to 15 patients were selected monthly to receive fully subsidised radiotherapy on the basis of predefined criteria, which included curability, age, and Eastern Cooperative Oncology Group (ECOG) performance status. All patients required an ECOG performance status ≤ 2 , both for prognostic purposes and because patients treated had to be ambulatory and capable of self-care, while undergoing their outpatient treatment regimens. The patient groups were accompanied on their nine-hour bus trip to Mulago by an oncology nurse, who would orient the patients in their hostel accommodation on arrival, as well as the clinical facilities at the hospital. In addition, the nurse would deliver their Rwandan Ministry of Health clinical referral documents to the UCI staff.

Of the 208 referred to Mulago, 160 (77%) had cervical cancer, 31 (15%) had head and neck cancer, and 17 (8%) had rectal cancer. At the time of data collection, 101 (49%) radiotherapy patients were alive and had completed treatment with no evidence of recurrence, 11 (5%) were alive and continuing treatment, 12 (6%) were alive and had completed treatment with evidence of recurrence, 26 (13%) were referred to palliative care for pain and symptom management at their district hospital, 30 (14%) were lost to follow up, and 19 (9%) were deceased. More than one half of the patients who received radiotherapy were alive with no evidence of recurrence at a median follow-up of 12 months, including 59% of all patients with cervical cancer. ▼



MARK LODGE

The authors point out that these outcomes compare favourably to a series of patients with cervical cancer in Kenya treated with radiotherapy (reported in 2013), which demonstrated an overall survival of approximately 50% at 15 months [4].

A retrospective costing analysis of BCCOE's cancer programme from the provider perspective conducted by Neal *et al* [5] identified Butaro's collaborative arrangement with Mulago hospital as being a significant cost driver for BCCOE. After start-up funding to implement the cancer programme at Butaro (assessed at US\$556,105) the annual operating cost of the cancer programme for the fiscal year 2013-2014 was found to be US\$957,203. All the costs for the year related to radiotherapy treatment in Uganda, including transport, medical bills, lodging, and meals totalled to be US\$236,444, representing 25% of the Centre's operating costs, compared with labour US\$198,5672 (21%) and chemotherapy, supportive medications, and consumables at US\$139,134 (15%). The per capita cost of providing the 208 patients with radiotherapy was US\$1136.75. Neal *et al* argue that taking into account the building, equipment, and human resources necessary to run the equipment, the initial investment for a basic radiotherapy clinic with two megavoltage units is estimated to be between US\$5-6 million. Amortised over the life of the clinic, the resultant cost might be between US\$250,000 and US\$400,000 annually. Rwanda's existing investment in radiotherapy was already close to the bottom end of this estimated annual investment.

The referral strategy at Butaro demonstrates the clinical feasibility of a rural cancer facility to conduct out-of-country radiotherapy referrals successfully, with promising early outcomes. At the same time the financial costs enumerated for radiotherapy services make a strong case for the development of local radiotherapy capacity in Rwanda.

Both Hanappe *et al* and Neal *et al* present the limitations of their analyses and that of the different courses of action fairly. Hanappe *et al* report that of the 272 patients excluded from referral to Mulago, 91 (33%) were lost to the study because they had missing paper records or records without a documented clinical or pathologic diagnosis. Initial presentation with advanced stages of disease remained a challenge, as did treatment delays due, in part, to the necessity of referring patients first to Kigali, because CT scan, endoscopy, surgery and other facilities were not available at BCCOE. The lack of a control group was a primary limitation of the BCCOE protocol and the unique factors in the cancer programme – the rural location at a single district hospital and the significant support from external funders (Ministry of Health Rwanda, Partners in Health, and Dana-Farber/Brigham and Women's Cancer Center) – mean that the Centre's experiences and outcomes may not have comprehensive external validity with respect to other resource-limited settings.

For their part, Neal *et al* remind us that it is important to take into account additional ongoing costs, such as machine maintenance, quality control and staff training when

considering the major investment of establishing a new radiotherapy centre in-country. Further, the perspective of their study was limited by its focus on capturing and analysing the costs of implementing an effective cancer programme. It did not include the larger societal costs of treatment, such as the out-of-pocket expenses of patients or lost productivity during treatment, or societal costs such as the time the patient spends away from home. The authors recognised that these potentially significant costs of treatment to the family and to society was not reflected in their study. Nevertheless, they argue that the costs enumerated for radiotherapy services make a strong case for the development of local radiotherapy capacity in Rwanda. With local radiotherapy services, a much higher number of patients could receive treatment than are currently receiving care for the existing investment.

Two recent developments indicate that their arguments will soon be put to the test. In their paper, Hanappe *et al* reported that in March 2016 – i.e. after the time of their data collection – patients from BCCOE had temporarily no longer been able to receive radiotherapy in Mulago because of the inoperability of the hospital's aged cobalt external-beam radiotherapy machine. As a consequence, patients were being transferred by air to Nairobi, Kenya, at increased expense. Unreliability of the referral service offered by Mulago had simultaneously raised the cost per patient and further limited the number of patients able to receive life-saving treatment. ▼

In December 2018 the announcement was made of the imminent opening of Rwanda's first radiation oncology centre at the Rwanda Military Hospital at Kigali, under the direction of Dr Pacifique Mugenzi, the only radiation oncologist in Rwanda. Built with the aid of a US\$3 million grant from the US government, and equipped with two linear accelerators from Elekta and the capacity to treat 80 patients per day, the new facility will be offering advanced treatment techniques with volumetric modulated arc therapy (VMAT). Radiation therapy services delivered at RMH will be available to Rwandans who use local insurance including *mutuelle de santé* (community health insurance).

Scheduled to open in January 2019, the RMH's Centre is intended to provide patients and their families with access to high cancer care as close to their home as possible and with further choice when planning their care, while reducing reliance on referrals to international centres.

The new Centre is seen as a great opportunity for Rwanda and its cancer patients, and possibly as a regional centre that might attract patients from surrounding countries [6]. However, its new Director General, Dr Mugenzi, has warned that while the new centre at RMH will increase access and affordability, by itself it cannot cover the entire population of Rwanda and the neighbouring countries in need of treatment, saying: "It is our hope that another centre will be open sooner rather than later." [7]

Despite their limitations, Hanappe *et al* and Neal *et al* have provided timely baseline data that may be used at a future date to compare the clinical

and cost benefits and implications of treating cancer patients resident in a low- or middle-income country setting with radiotherapy at home or abroad.

Mark Lodge
International Network for Cancer Treatment and Research (INCTR)
Oxford, UK

REFERENCES

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RESEARCH PROJECTS



RESEARCH PROJECTS

European Alliance fosters research in medical radiation protection and welcomes medical research centres and university hospitals

The European Alliance for Medical Radiation Protection Research (EURAMED) was established by five medical associations involved in the application of ionising radiation in medicine: the European Association of Nuclear Medicine (EANM), the European Federation of Organisations for Medical Physics (EFOMP), the European Federation of Radiographer Societies (EFRS), the European Society of Radiology (ESR) and ESTRO. EURAMED's goal is to improve medical care and promote medical radiation protection through research. Since 1 October 2017, EURAMED has been a non-profit organisation registered in Austria. EURAMED is currently led by Professor John Damilakis from Heraklion, Greece. Professor Damilakis took over leadership from Professor Christoph Hoeschen from Magdeburg, Germany, who orchestrated the development of EURAMED prior to its establishment as a legal entity. EURAMED's management is conducted by the European Institute for Biomedical Imaging Research (EIBIR).

EURAMED complements existing European platforms in several other fields of radiation protection, including the:

- Multidisciplinary European Low Dose Initiative (MELODI)
- European Radiation Dosimetry Group (EURADOS)
- European Platform for Nuclear and Radiological Emergency Response and Recovery (NERIS)
- European Radioecology Alliance (ALLIANCE).

EURAMED's overall vision is to lead European research activities in medical radiation protection and to assume an umbrella function for the harmonisation of practice with the goal of advancing European radiation protection safety culture in medicine. Specifically, EURAMED's mission is to:

- improve medical care through research in medical radiation protection
- identify common areas for research in a common strategic research agenda
- serve as a platform for medical radiation protection research, linking researchers and clinicians, adopting a harmonised approach to lobbying at European level to influence the European research funding landscape
- develop aligned approaches and responses to European research calls.

EURAMED seeks to achieve this by promoting research and teaching and by publishing scientific and professional information, especially its strategic research agenda for the field of medical radiation protection research. Through this work, EURAMED is increasing the scientific basis for medical radiation protection.

EURAMED co-operates with relevant national, European and international scientific organisations and, in particular, with national and international bodies promoting medical radiation protection research. In addition to this, EURAMED intends to work with patient organisations and the public at large. ▼



WOLFGANG DÖRR

EURAMED's activities

Since becoming a legal entity on 1 October 2017, EURAMED's work has included:

participation in the International Symposium on the System of Radiological Protection European Radiological Protection Research Week (ICRP-ERPW 2017) in Paris, France, and the European Radiation Protection Week in Rovinj, Croatia, in October 2018, including several sessions dedicated to the medical field.

EURAMED also engaged in a joint road mapping exercise led by the CONCERT project, which EURAMED joined as a project partner in 2018. EURAMED initiated its own roadmap development, for which a working group has been established with representatives from EURAMED's five founding societies, whose input is currently being collected.

The joint roadmap led by the CONCERT project is seen as a guide for future strategies and funding in this field. The mapping exercise showed four contexts for which radiation protection may be required:

- i) human activities related to medical therapy and diagnosis using radionuclides and x rays, protons or ions
- ii) human activities related to nuclear energy applications and other industrial applications for ionising radiation not related to medical applications
- iii) human activities related to the use of natural resources, containing naturally occurring radionuclides (NORM / TENORM)

iv) natural radiation as source of ionising radiation.

The exercise defined 'optimised radiation protection in medical applications of ionising radiation' as one of the major challenges in radiation protection research and development.

Furthermore, EURAMED has been approved as an International Commission on Radiological Protection (ICRP) Special Liaison Organisation and presented its mission and activities at an ICRP meeting in October 2018.

EURAMED has encouraged the medical community to develop research proposals for the Euratom 2018 calls and has itself participated in the SERENADE project proposal, addressing the subject matter of the call: 'Strategy for the exploitation of research results funded under Euratom research and training programmes in the field of radiation protection.'

In 2019, EURAMED will participate in the International Atomic Energy Agency's (IAEA) International Symposium on Standards, Applications and Quality Assurance in Medical Radiation Dosimetry (IDOS 2019). IDOS 2019 aims to provide a forum in which advances made in radiation dosimetry, radiation medicine, radiation protection and associated standards over the past decade can be disseminated and scientific knowledge exchanged. It will take an active role in the 2019 European Radiation Protection Week to be held

in Stockholm, Sweden, and aims to publish its research roadmap in the course of the year.

Join EURAMED

One of EURAMED's key goals for this year is to expand its membership, which will help to strengthen the activities of its committees and working groups.

Membership is available in the following categories:

- full member (institutions or organisations active in the field of medical radiation protection research)
- associate member (institutions or organisations that do not actively practice medical radiation protection research, but which have a considerable interest in the area of radiation protection)
- corporate member (enterprises interested in the activities and aims of the society)
- individual member (any health professional or other scientist committed to the objectives of EURAMED with a university or equivalent education may apply for individual membership of EURAMED, provided that they are engaged in radiology, nuclear medicine, radiation oncology, medical physics, radiography or related fields).

Member recruitment has started and is a current priority. Membership is designed to be particularly attractive to medical institutions, radiation protection institutions, and authorities interested in medical radiation protection. ▼

The focus of EURAMED is necessarily on the medical aspects of radiation protection, which is why medical research centres and university hospitals should be especially suited to becoming full members.

Wolfgang Dörr
ESTRO representative in EURAMED



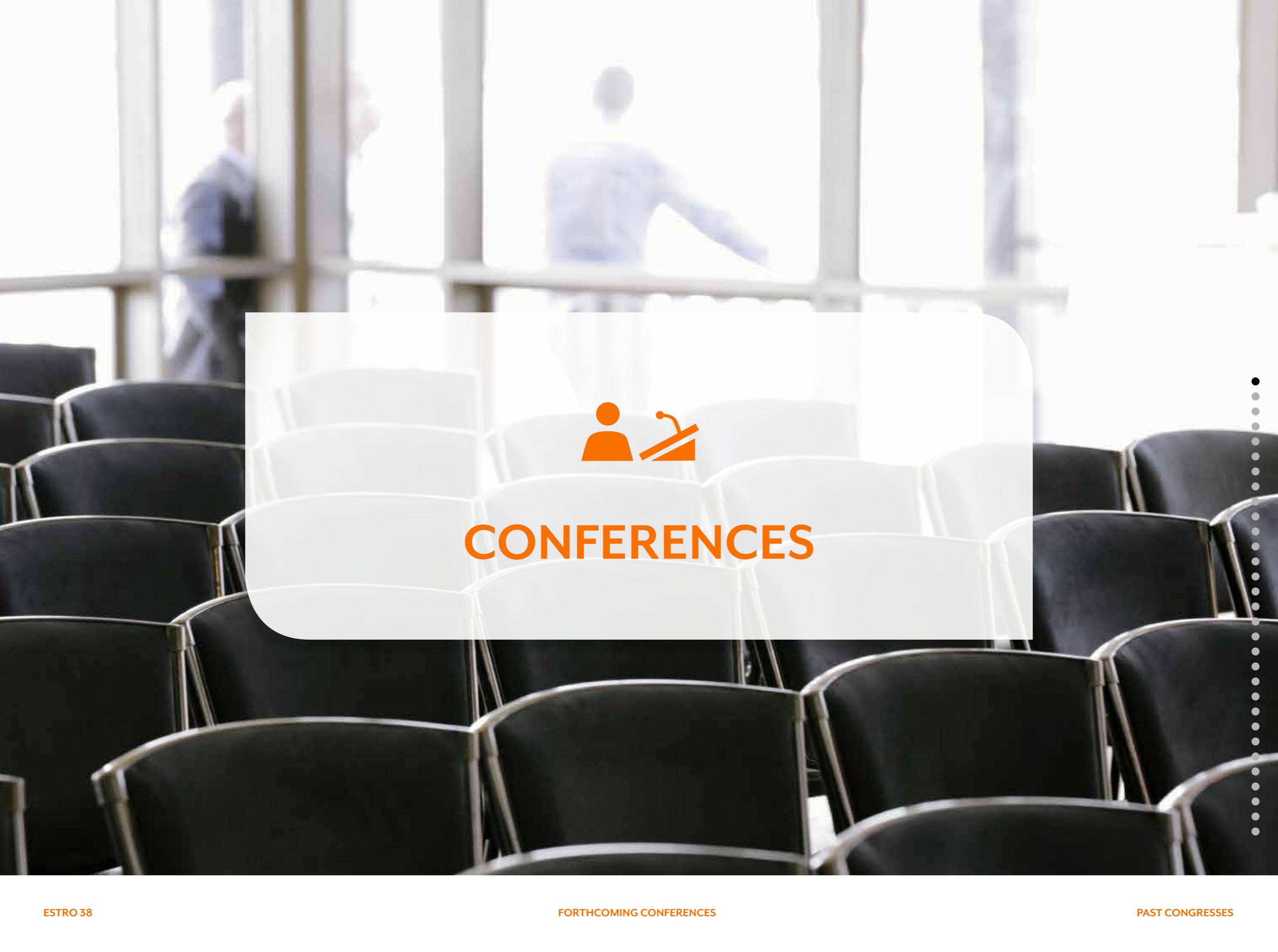
**For more information and to
apply for membership, visit:**
www.euramed.eu

5th European Particle Therapy Network (EPTN)

9 April 2019 | Brussels, Belgium

REGISTRATION IS OPEN!

**[www.estro.org/congresses-meetings/
items/5th-european-particle-therapy-
network-eptn](http://www.estro.org/congresses-meetings/items/5th-european-particle-therapy-network-eptn)**



CONFERENCES



7TH ICHNO

International Congress on
innovative approaches in

HEAD & NECK ONCOLOGY

14-16 March 2019

Barcelona, Spain

Early registration deadline:

6 November 2018

WWW.ESTRO.ORG

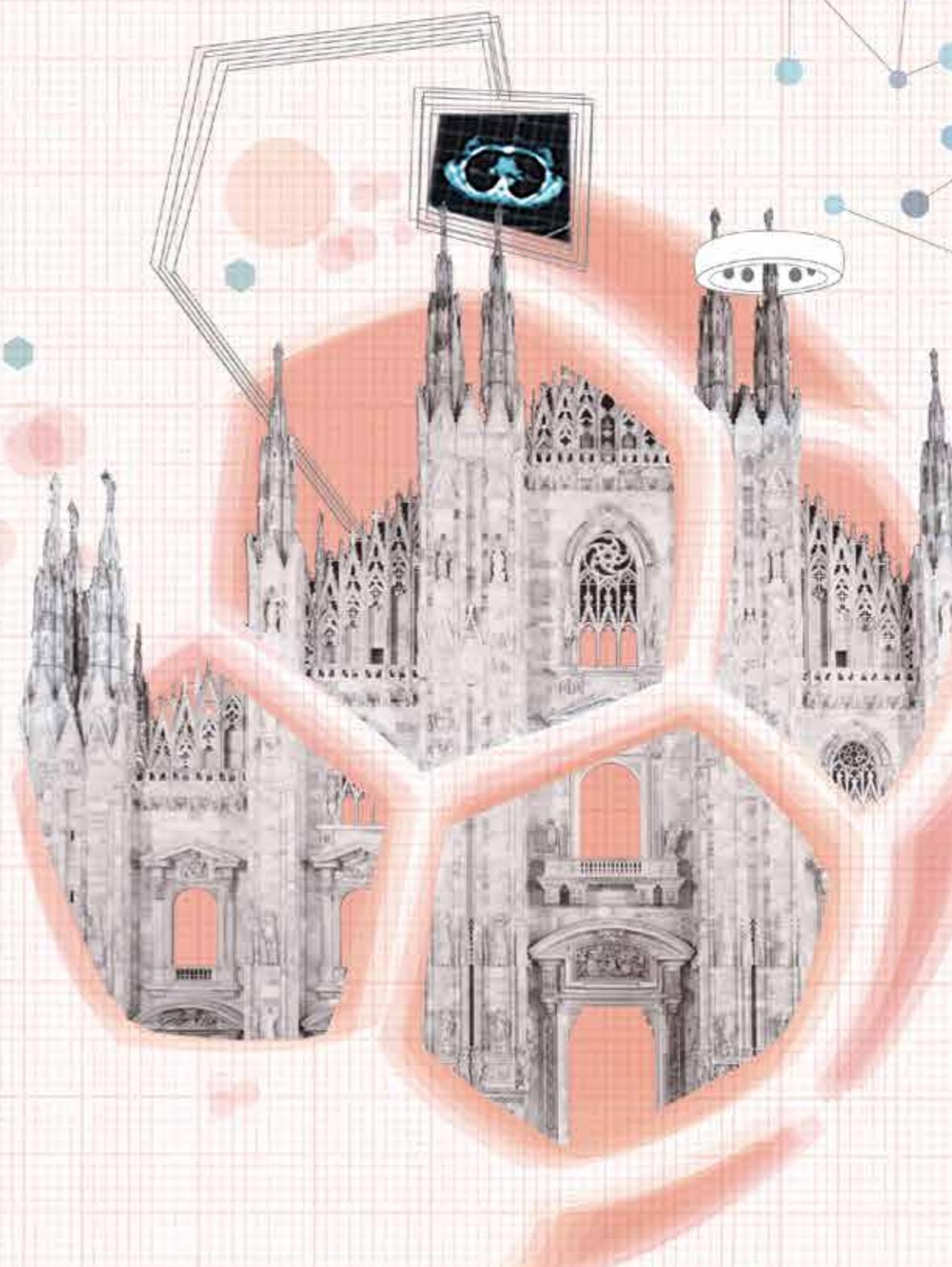
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ESTRO 38

26-30 April 2019
Milan, Italy

Targeting
optimal care,
together





Interview with ESTRO 38 track chairs

Clinical – Claus Rödel ▶▶

Brachytherapy – Bradley Pieters ▶▶

Physics – Catharine Clark ▶▶

RTT – Bartosz Bak ▶▶

Radiobiology – Marc Vooijs ▶▶

Communities Pavilion ▶▶

ESTRO 38 Joint sessions ▶▶

ESTRO 38 in figures ▶▶

Mark your calendar ▶▶



Interview with ESTRO 38 Clinical track chair

Claus Rödel

Goethe University of Frankfurt,
Frankfurt, Germany



CLAUS RÖDEL

What are the trending topics in the abstracts you received?

A continuing trend for individualised radiation therapy is evident. In the era of ‘personalised’ medicine, radiation oncologists now increasingly adapt their treatment strategies based on molecular sub-classifications and/or functional imaging and radiomics. Also, a number of abstracts relate to the use of combinations of radiotherapy with targeted agents, including immune modulation, for various tumour entities within prospective phase I/II clinical trials. Another emerging topic is MR-guided adaptive radiation and high-precision radiotherapy, including stereotactic body radiation therapy (SBRT) for treating oligometastatic disease, and the use of particle therapies for paediatric and/or more radio-resistant tumours. In addition, a better understanding and prediction of long-term adverse side-effects (e.g. of cardiac or neurocognitive sequelae) is the focus of several excellent clinical abstracts.

Do some of the abstracts present innovative methods of research?

An innovative, double-blind randomised trial tested parotid gland stem cells sparing

intensity-modulated radiation therapy (IMRT) for head and neck patients in an effort to reduce xerostomia. Another group shows that response to radiotherapy in soft-tissue sarcoma can be significantly increased by an intra-tumoural injection of hafnium oxid nanoparticles that are activated by ionising radiation, yielding an intra-tumoural high energy deposit. As an ongoing international project, the REQUITE prospective cohort study continues to gather comprehensive clinical data with a linked biobank for patients who received radiotherapy for breast, lung and prostate cancer. This centralised database will provide a large and valuable platform for validating models and biomarkers to predict late effects of radiotherapy and quality-of-life.

Are there any studies that particularly caught your attention?

Yes, the large national and international groups will be presenting their randomised data at ESTRO 38. These include the 10-year results of the ABCSG 8A trial on anti-hormonal treatment with or without whole breast irradiation in low-risk breast cancer; the seven-year results from the HYPRO trial of conventional versus hypofractionated radiotherapy for intermediate to high-risk prostate cancer; and the five-year ▼



results of the GRECCAR2 organ preservation trial of chemoradiotherapy, followed by local excision, versus total mesorectal excision surgery in early rectal cancer patients.

Do you have any other comments?

It is encouraging to see how many prospectively controlled clinical phase I to III trials have been designed, completed and now provide long-term results within Europe. As radiation oncologists it is reassuring to see that we continue to provide high-level evidence for the use of radiation therapy as curative and effective palliative treatment within multimodality approaches.





Interview with ESTRO 38 Brachytherapy track chair

Bradley Pieters

Academic Medical Centre,
Amsterdam, The Netherlands



BRADLEY PIETERS

What are the trending topics in the abstracts you received?

The highlight this year is a paper from Hannah Tharmalingam *et al* that comprises a UK-wide study on single dose 19 Gy high dose rate (HDR) for prostate cancer. This schedule is shown to be safe and effective with good early biochemical control. Low acute toxicity rates are also found for a one-day HDR schedule by Marjory Jolicoeur *et al*. However, Alfonso Gomez-Iturriaga *et al* find a high recurrence rate with a 19 Gy single dose schedule, especially for intermediate-risk patients. The value of this single dose treatment is still a matter of debate and needs to be investigated further.

Salvage prostate brachytherapy is another topic that is addressed by several groups. The results of this emerging treatment show that it is becoming a standard treatment option. Max Peters *et al* show in a study of 96 patients treated with a single dose of 19 Gy that focal salvage brachytherapy leads to high tumour control with low severe toxicity rates. Other papers show the same results. The study of Piotr Lelek *et al* is different from the other studies due to its longer follow-up time. Salvage brachytherapy (3 x 10 Gy) resulted in a five-year biochemical failure-free survival of 59%.

Accelerated partial breast implantation (APBI) is investigated by several groups (Kellas-Slecicka *et al*, Cihoric *et al*). All these studies show that in selected cases APBI is a safe procedure leading to good local control. The good news is that these mono-centre studies also confirm the very positive results of the GEC-ESTRO APBI study.

This year a whole session is being dedicated to treatment verification. Several authors are presenting their work on electro-magnetic tracking for verification of source position during dose delivery. Others have focused their investigation on *in vivo* dosimetry to verify the actual dose given during treatment.

Do some of the abstracts present innovative methods of research?

In the paper by Anton Bouter *et al* prostate treatment plans were generated by performing bi-objective optimisation with evolutionary algorithms leading to fast and high-quality treatment plans.

Are there any studies that particularly caught your attention?

A study that caught my attention is the study ▼



on second breast conserving treatment for breast cancer by Jean-Michel Hannoun-Levi. This is a study from the GEC-ESTRO breast working group involving 331 patients. It shows that a second breast conserving treatment with brachytherapy is feasible with good local control and low toxicity rate.

Do you have any other comments?

I would like to thank all authors, speakers, session chairs, members of the scientific advisory group, abstract reviewers and the ESTRO office for their dedication and work to help make the Brachytherapy Track at ESTRO 38 a success.





Interview with ESTRO 38 Physics track chair

Catharine Clark

Royal Surrey County Hospital,
Guildford, UK

National Physical Laboratory,
Teddington, UK



CATHARINE CLARK

What are the trending topics in the abstracts you received?

This year there has been a big increase in the number of abstracts on radiobiological predictive modelling and radiomics, and adaptive radiotherapy and inter-fraction motion management. There are also lots of submissions on protons across all topics, but especially in planning, measurement and toxicity, showing that the implementation of proton treatment in Europe is really taking off. There is also a significant increase in the use of MRI in pre-treatment planning, intra-fraction motion management and radiomics.

Do some of the abstracts present innovative methods of research?

There is a fascinating study on a trial established to investigate the role of gut/saliva microbiota in radio-induced toxicity after treatment for prostate cancer by Rancanti *et al.* Evaluation before, during and after radiotherapy suggests that patients with radio-induced acute toxicity have different constitutional gut microbiota profiles.

Are there any studies that particularly caught your attention?

A couple of submissions caught my attention for the way in which they push the field forward by combining several recent developments for the benefit of patients. The first is by Barragan *et al.* This study looks at MRI-only proton treatment planning with synthetic CT images generated using deep learning. The study used neural networks to quickly generate and then validate the conversion to CT from MR images. These converted images were then used for proton planning. The differences between the plans using the synthetic image and the original CT were minimal, suggesting that the synthetic CT could be used alone.

The other study is on real-time reconstruction of the delivered dose to a moving tumour during radiotherapy delivery by Skouboe *et al.* The authors monitored liver stereotactic body radiation therapy (SBRT) patients treated using volumetric modulated arc therapy (VMAT). They used implanted gold markers and continuous monitoring of an external marker combined with x-ray images acquired by a gantry-mounted imager. The tumour position was streamed to an in-house programme that reconstructed the actual motion-including dose. ▼



This work is a significant step towards real-time monitored radiotherapy with important potential applications for real-time quality assurance (QA) and dose-guided treatment adaptation.

Do you have any other comments?

I was particularly interested to see the number of studies that used multi-centre data either for outcome and toxicity assessment or for analysis of quality. This really highlights how we are working together more closely as a community to assess the approaches we are taking on a large scale and sharing the best ways to treat our patients more effectively and efficiently.





Interview with ESTRO 38 RTT track chair

Bartosz Bąk
Greater Poland Cancer Centre,
Poznan, Poland



BARTOSZ BĄK

What are the trending topics in the abstracts you received?

The most popular topics relate to adaptive radiotherapy. For a number of years now the main theme of congress abstracts has been personalisation of treatment plans, dose reduction and the best/quickest possible adaptation of treatment. Once again, we have received a lot of abstracts on these topics this year, focusing on the control and compensation systems for intra- and inter-fraction organ motion.

Abstracts concerning MR linac and proton therapy research are also popular. There are many reports on immobilisation, verification and adaptation of treatment, and RTT responsibility in the clinical workflow.

Some papers describe new approaches in respiratory control systems using virtual reality systems. Virtual reality and hypnosis-based stress management strategies are already showing encouraging results in a number of medical fields.

Do some of the abstracts present innovative methods of research?

The number of papers submitted for the RTT Track at ESTRO 38 has increased again: 162 abstracts from 33 countries have been submitted. As in previous years, abstracts on a range of topics were submitted from countries outside Europe.

The highly scored categories focused mainly on topics related to motion management and adaptive strategies, patient care, side effects and communication, imaging acquisition and registration, organs at risk (OAR) and target definition, and improving accuracy in patient positioning.

Are there any studies that particularly caught your attention?

The RTT scientific advisory group selected the following three studies:

- Webster *et al* present the first international multi-centre trial assessing whether RTTs correctly implement the plan of the day for radical bladder radiotherapy.
- Rianne de Jong *et al*'s paper on image-guided adaptive radiotherapy. ▼

Researchers analysed target coverage and dose to the organs at risk for the clinically used adaptive plan selection strategy compared to a non-adaptive approach for both short (5x5Gy) and long (25x2Gy) treatment schedules for rectal cancer patients.

- Duffton *et al*'s paper concerning the use of MRI to determine threshold change in the apparent diffusion coefficient (ADC), which distinguishes responders from non-responders in radiotherapy.





Interview with ESTRO 38 Radiobiology track chair

Marc Vooijs

Maastricht University

Maastricht, The Netherlands



MARC VOOIJS

What are the trending topics in the abstracts you received?

There is an increase in immunotherapy and normal tissue studies, particularly pre-clinical studies on neurocognition and several genome-wide biomarker studies for normal tissue toxicity. This year there seems to be a reduction in the number of abstracts studying DNA repair.

Do some of the abstracts present innovative methods of research?

There are several novel preclinical tumour models combined with precision irradiation using photons as well as particles. Several abstracts describe the effects of radiation on tissue-specific stem cells.

Are there any studies that particularly caught your attention?

There are many interesting studies, but some examples include:

- An analysis of biomarkers for late radiotherapy toxicity in the REQUITE project (Christopher Talbot *et al*)
- The results of a large prospective study with more than 4,000 patients to predict

radiotherapy toxicity (REQUITE)

- Targeting TEMPRSS2: ERG fusion to achieve a tumour-specific radiosensitisation in prostate cancer (Wael Mansour *et al*). This study identifies vulnerability for combining PARP inhibition and radiation in ERG-over-expressing prostate cancers in preclinical and patient studies.
- A study on the immunological contexture basis of a prognostic radiomics signature in head and neck cancers (Dan Ou *et al*). This study analysed a large number of CT images from patients with head and neck cancer and correlated a prognostic radiomics signature and HPV status with immune infiltration phenotype in these tumours using immunohistochemistry (IHC) from biopsies.

Do you have any other comments?

There was an almost two-fold reduction in the number of submitted abstracts for the radiobiology track at ESTRO 37. While the number of abstracts submitted in this area has fluctuated over the years it is important that we continue to attract biologists to our large interdisciplinary meeting. At ESTRO 38, for the first time, we have organised a joint symposium with the European Association ▼



of Cancer Research to ensure that we take a broad perspective on developments in radiotherapy. The radiobiology committee is considering how to increase further the number of biologists attending the ESTRO congress. We encourage you to bring ESTRO to the attention of your colleagues in your institutes as well, and we would welcome any suggestions for improvements.





2019 ESTRO Communities Pavilion

26-30 April 2019
Exhibition area



At ESTRO 38, all delegates will be invited to the Communities Pavilion. Designed to foster exchanges about science, projects, collaborations, and why not, job opportunities, the Communities Pavilion provides a networking forum for the wide range of stakeholders in radiation oncology.

Launched in 2017, the Communities Pavilion welcomes institutions, national societies as well as patient associations, each represented within one booth. The ESTRO Communities Pavilion is open to all ESTRO 38 participants. The following organisations may participate as exhibitors:

- All institutes
- National societies
- International radiotherapy societies
- Patients associations
- Other oncology associations

Opening hours

Friday 26 April at 19:00. It will remain open from Saturday 27 April to Monday 29 April 09:30-17:00 hrs. For more information, please contact: Gabriella Axelsson (gaxelsson@estro.org)

ESTRO 38 Joint Sessions

This year ESTRO 38 will include a number of joint sessions that will highlight the collaboration among professionals in the oncology area. The participating organisations are: The American Association of Physicists in Medicine (AAPM), the American Society of Radiotherapy and Oncology (ASTRO), the European Association for Cancer Research (EACR), the European Federation of Organisations for Medical Physics (EFOMP), the European Organisation for Research and Treatment of Cancer (EORTC), the European Society of Radiology (ESR), the International Atomic Energy Agency (IAEA), the Japanese Society of Radiotherapy and Oncology (JASTRO), the Royal Australian and New Zealand College of Radiologists (RANZCR).

ESTRO-AAPM

QA of on-line adaptive radiotherapy

Saturday 27 April 2019 | Space 1-2 | 8:45 - 10:00 hrs



ESTRO-EFOMP

Multi-disciplinary working in Radiotherapy

Saturday 27 April 2019 | Space 3-4 | 14:30 - 15:45 hrs



ESTRO-JASTRO

Clinical trials for particle therapy: which ones to run and how?

Sunday 28 April 2019 | Auditorium | 10:30 - 11:45 hrs



ESTRO-ASTRO

Translating discovery to cure

Sunday 28 April 2019 | Auditorium | 16:15 - 17:30 hrs



ESTRO-ESR

Current status and future challenges in MR-integrated radiotherapy

Monday 29 April 2019 | Gold Plenary | 8:45 - 10:00 hrs



ESTRO-EACR

Radio-immunotherapy: from concept to clinical practice

Monday 29 April 2019 | Ambra 5-6 | 8:45 - 10:00 hrs



ESTRO-IAEA

The role of hypofractionation in current radiotherapy and its impact in planning radiotherapy services

Monday 29 April 2019 | Auditorium | 10:30 - 11:45 hrs



ESTRO -EORTC

Moving Radiation Oncology Forward to Improve Patient Outcomes

Monday 29 April 2019 | Brown 3 | 14:30 - 15:45 hrs



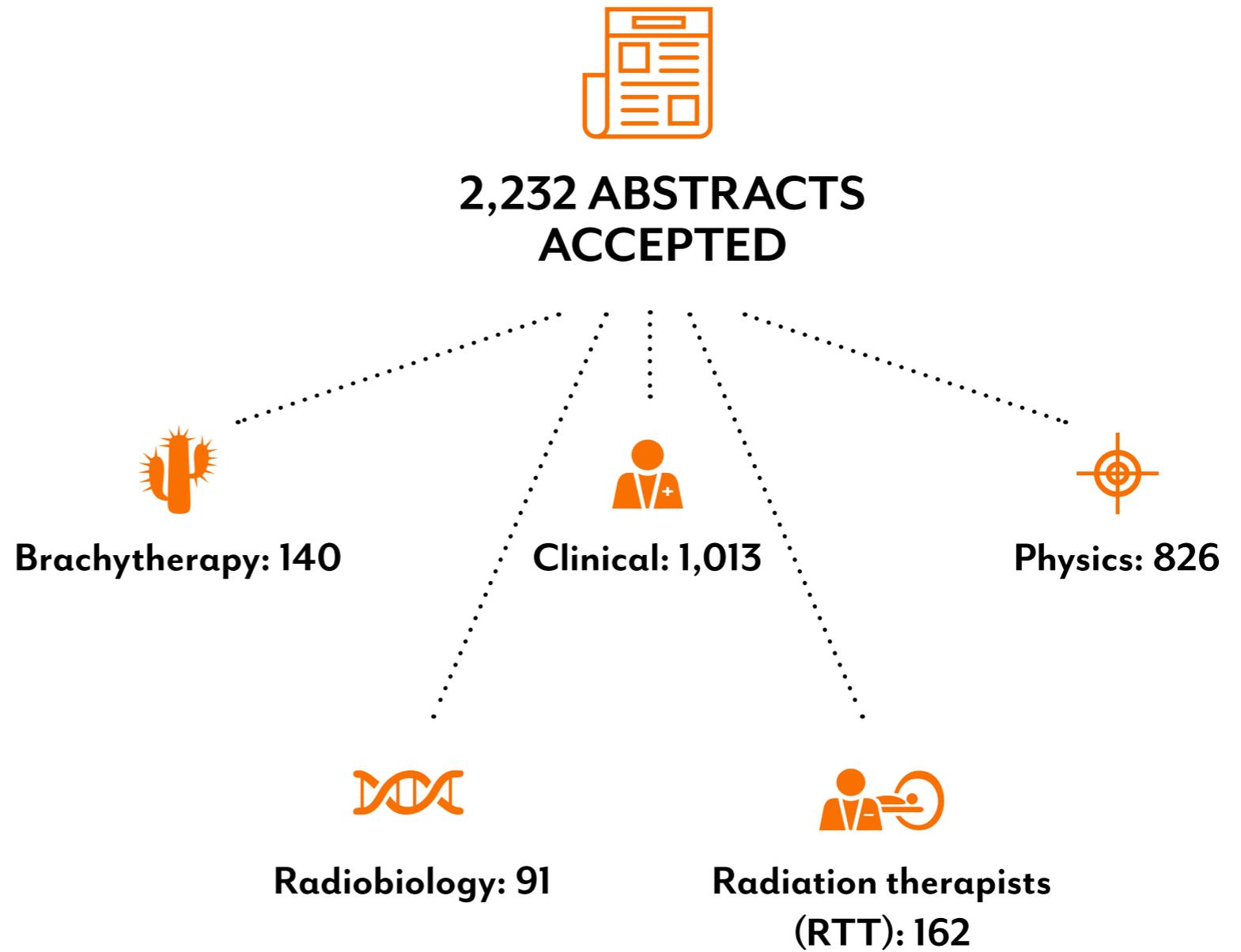
ESTRO-RANZCR

Radiotherapeutical management of oligometastatic disease

Tuesday 30 April 2019 | Ambra 5-6 | 11:00 - 12:15 hrs



ESTRO 38 in figures



ESTRO 38 DEADLINES

Late registration:
26 March 2019

Desk registration:
from 27 March 2019

Mark your calendar

Here is an overview of the important activities that are not to be missed during the congress.

Check out the latest available information on www.estro.org

One month before the Congress you will be able to access online the:

- Searchable programme
- Programme book
- Abstract book.

And, of course, follow us on Facebook, LinkedIn and Twitter (#ESTRO38) to hear the latest developments.

SOCIAL ACTIVITIES

Opening ceremony

Friday 26 April 2019

We can't wait to welcome you to Milan for a thrilling ESTRO 38, which will start on Friday 26 April 2019 with an opening ceremony. We recommend you book your travel accordingly!

Networking evening

Friday 26 April 2019

All registered participants and all company delegates are invited to the Networking evening which will take place in the exhibition area.

Awards ceremony

Saturday 27 April 2019

All participants and company delegates are invited to the poster awards ceremony, which will be held in the poster area.

Tweet-up

Saturday 27 April 2019

Meet your Twitter friends and network at the Tweet up taking place on Saturday 27 April in the poster area. Let's Tweet-up there!

Super Run

Sunday 28 April 2019 | 19:00 hrs

The Super Run has now become a not-to-be-missed event at the ESTRO annual meetings. The initiative brings together congress participants and cancer patients to run to raise awareness of radiotherapy, and also to underline the importance of sport for good health. Don't forget to pack your running shoes! Registration will open mid-february.

After dinner event

Monday 29 April 2019 | 21.30 hrs

All participants are invited to an after-dinner event which will take place in Alcatraz in Milan.

POST CONGRESS TOUR

Tuesday 30 April | 13.45 hrs

ESTRO will organise a post congress tour to the Fondazione CNAO (National Center of Oncological Hadrontherapy for the treatment of tumours) on 30 April.

Enter the bunker of the synchrotron, an 80 meters long particle accelerator, where carbon ions and protons travel, and be amazed in front ▼

of the robotic system for positioning the patient in the treatment rooms of CNAO. Physicists, engineers and technicians from CNAO will take you along a route of about 1 ½ hour.

Busses will leave from the MiCo at 13:45 hrs and will be back at around 16.45 hrs.

YOUNG TRACK

Sunday 28 April 2019 | 17.00 hrs

The young scientists' sessions

AWARDS

Lifetime Achievement

Gyorgy Kovacs

Ekkehard Dikomey

Riccardo Calendrini

Christian Carrie

ESTRO Award lectures and Academic Awards

Emmanuel van der Schueren Award Lecture

Núria Jornet (Spain)

Saturday 27 April from 12:00 to 12:30 hrs

Gold Plenary

Learning from clinical practice: pushing quality forward

Iridium Award Lecture

Christine Haie-Meder (France)

Saturday 27 April from 12:30 to 13:00 hrs

Gold Plenary

The role of women in the brachytherapy field

Honorary Members award lectures

Giorgio Scagliotti (Italy)

Saturday 27 April from 17:35 to 17:50 hrs

Gold Plenary

Multidisciplinary approaches as the keys to defeat lung cancer

Honorary Members award lectures

Julie Torode (Switzerland)

Saturday 27 April from 17:50 to 18:05 hrs

Gold Plenary

Are radiation specialists good global cancer citizens?

Honorary Members award lectures

Angelita Habr-Gama (Brazil)

Saturday 27 April from 18:05 to 18:20 hrs

Gold Plenary

Putting down the scalpel. The evolution of rectal cancer treatment.

Claudius Regaud award Lecture

Dirk De Ruysscher (The Netherlands)

Sunday 28 April from 12:30 to 13:00 hrs

Gold Plenary

Is fractionation history?

Honorary Physicist Award Lecture

Matthias Guckenberger (Switzerland)

Sunday 28 April from 18:00 to 18:20 hrs

Gold Plenary

Precision medicine – an opportunity for medical physics and radiation oncology

Klaus Breur Award Lecture

Vincenzo Valentini (Italy)

Monday 29 April from 12:00 to 12:30 hrs

Gold Plenary

A stroll in Rome together





Academic award: Jack Fowler University of Wisconsin Award

Simon Skouboe (Denmark)

Monday 29 April from 12:30 to 12:40 hrs

Gold Plenary

First clinical real-time motion-including tumor dose reconstruction during radiotherapy delivery

Donald Hollywood award lecture

Roel Steenbakkers (The Netherlands)

Monday 29 April from 17:40 to 17:50 hrs

Gold Plenary

Stem cell sparing IMRT for head and neck cancer patients: a double-blind randomized controlled trial

Jens Overgaard Legacy Award

Philip Poortmans (France)

Sunday 28 April from 17:40-18:00 hrs

Gold Plenary

TBC

Company awards

GEC-ESTRO Best Junior presentation sponsored by Elekta Brachytherapy

Max Peters (The Netherlands)

Sunday 28 April from 11:00 to 11:10

Brown 2

Clinical outcomes of focal salvage high-dose-rate brachytherapy for radiorecurrent prostate cancer.

ESTRO-Elekta Brachytherapy award

Anton Bouter (The Netherlands)

Sunday 28 April from 16:25 to 16:35

Brown 2

Bi-objective optimization of dosimetric indices for HDR prostate brachytherapy within 30 seconds

ESTRO-Varian Award

Timo Deist and Frank Dankers (The Netherlands)

Monday 29 April from 12:40 to 12:50

Gold Plenary

Distributed learning on 20 000+ lung cancer patients

**EIGHT PRE-MEETING COURSES
FRIDAY 26 APRIL 2019**

Clinical pre-meeting course:

MR-guided radiotherapy for clinicians

Course directors: B. Slotman (The Netherlands) and C. Gani (Denmark)

Course aim

To provide an overview of the current and potential role of external beam MRI guided radiotherapy for clinicians.

Read the full description: www.estro.org/congresses-meetings/articles/estro-38---pre-meeting-clinical

Interdisciplinary pre-meeting course:

Conservative treatment in early rectal cancer

Course directors: N. Gambacorta (Italy) and A. Appelt (UK)

Course aim

To provide an overview of the alternatives to radical surgery in the management of rectal cancer, including patient selection, imaging, pathology and radiotherapy techniques. ▼



Read the full description: www.estro.org/congresses-meetings/articles/estro-38---pre-meeting-interdisciplinary

Management of high-risk prostate cancer

Course directors: A. Bossi (France) and G. De Meerleer (Belgium)

Course aim

To provide an up-date of the current challenges related to the diagnosis and management of High Risk prostate cancer patients with specific emphasis on the role of EBRT and brachytherapy, whether or not within a multimodality approach. Read the full description: www.estro.org/congresses-meetings/articles/estro-38---pre-meeting-management-of-high-risk-prostate-cancer

Physics pre-meeting course:

Machine Learning for Physicists

Course directors: B. Heijmen (The Netherlands) and D. Verellen (Belgium)

Course aim

To provide basic knowledge on machine learning and its potential use in Radiation Oncology.

The course aims at enabling medical physicists to understand the basics behind clinical applications from a user point of view and, provide information for interested developers to get started without prior knowledge. The course assumes that the participants have no knowledge on the subject.

Read the full description: www.estro.org/congresses-meetings/articles/estro-38---pre-meeting-physics

Basic course brachytherapy treatment

Course directors: R.I. Schokker (The Netherlands) and B. Wisgrill (Austria)

Course aim

Radiation Therapist (RTTs), dosimetrists and RT nurses have several tasks in the brachytherapy treatment. To get to a more uniform level of knowledge, this course will provide with the basic principles of brachytherapy. Next, to these basic principles, there will be different hospitals from various European countries presenting their workflow. It will be an interactive program, where participants can share their experiences. Read the full description: www.estro.org/congresses-meetings/articles/estro-38---pre-meeting-basic-course-brachytherapy-treatment

Radiobiology pre-meeting course:

Radiation induced cell death (the good and the ugly)

Course directors: F. Paris (France) and R. Coppes (The Netherlands)

Course aim

To provide insight in cellular processes leading the response to radiation.

Read the full description: www.estro.org/congresses-meetings/articles/estro-38---radiobiology-pre-meeting-course

Education pre-meeting course:

Foundations of leadership in radiation oncology

Joint ESTRO-CARO-RANZCR

Course directors: K. Benstead (UK), M. Giuliani (Canada), S. Turner (Australia)

Course duration: 8 weeks with live pre-meeting workshop at ESTRO 38:

- Online programme to start on 20 March 2019
 - Live session on 26 April and two lunch meetings
- Read the full description: www.estro.org/congresses-meetings/articles/estro-38---pre-meeting-foundations-of-leadership ▼

Education pre-meeting course:

Academic entrepreneurship and technology transfer in radiation oncology: dream or reality?

Course directors: *P. Lambin (The Netherlands) and K. Tanderup (Denmark)*

Course aim

Radiotherapy is a discipline involving a high degree of technology and using various discipline (imaging, biology, computer sciences, clinic, physics...). This course is meant as a workshop to stimulate collaboration between academia and industry and technology transfer which is essential for new technology to bridge the “second translational gap” and reach the patients.

Read the full description: www.estro.org/congresses-meetings/articles/estro-38---pre-meeting-academic-entrepreneurship

CONTOURING WORKSHOPS

FALCON (Fellowship in Anatomic DeLineation and CONtouring) is the multifunctional ESTRO platform for contouring and delineation. Eight such workshops have been planned for ESTRO 38.

Oar on head and neck cancer

Friday 26 April 2019 | 08:00-10:00
(repeated Saturday 27 April | 14:30-16:30)

Chair: J Cacicedo

Panellist: AR Lopes Simões (UK)

Rectal cancer

Friday 26 April 2019 | 10:30-12:30
(repeated Sunday 28 April | 14:30-16:30)

Chair : MA Gambacorta (Italy)

Panellists: C Valentini (Denmark)

Lung sbrt

Friday 26 April 2019 | 13:30-15:30
(repeated Monday 29 April | 14:30-16:30)

Chair: M. Dahele (The Netherlands)

Panellists: M Guckenberger (Switzerland) and A Navarro Martin (Spain)

Primary vaginal cancer

Friday 26 April 2019 | 16:00-18:00
(repeated Tuesday 30 April | 09:15-11:15)

Chairs: L Fokdal (Denmark) and H Westerveld (The Netherlands)

Panellists: R Nout (The Netherlands)

RENDEZ-VOUS WITH COLLEAGUES: ASSEMBLIES / MEET AND GREET

Radiobiology Meet and Greet

Saturday 27 April | 12:00-13:00 | Open space area of Exhibition

GEC-ESTRO Assembly

Saturday 27 April | 13.30-14.30 | Room Brown 2

Women in medical physics Meet and Greet

Sunday 28 April | 8:00-9:00 | Open space area of Exhibition

RTT Alliance Meet and Greet

Sunday 28 April | 10:30-11:30 | Open space area of Exhibition

RTT Meet and Greet

Monday 29 April | 12:00-13:00 | Open space area of Exhibition ▼



Physics Assembly

Monday 29 April | 13:30-14:30 | Room Brown 1

ESTRO General Assembly

Monday 29 April | 18.40-19.40 | Room Brown 2

WIFI

Wi-Fi will be available in all meeting rooms. Feel free to share information from the conference on social media and on Twitter using the hashtag #ESTRO38.



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Download the app from www.estro.org



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FORTHCOMING CONFERENCES

In collaboration with ESTRO

16th St Gallen International Breast Cancer Conference ▶▶

20-23 March 2019 | Vienna, Austria

Predictive models in external beam radiotherapy ▶▶

25-27 March 2019 | Naples, Italy

The 14th International Netherlands Cancer Institute Head and Neck Symposium Diagnosis and treatment of head and neck cancer: locally advanced tumours ▶▶

4-5 April 2019 | Amsterdam, The Netherlands

ESHO 2019: 33rd annual meeting of the European Society for Hyperthermic Oncology (ESHO) ▶▶

22-24 May 2019 | Warsaw, Poland

16th St Gallen International Breast Cancer Conference

20-23 March 2019
Vienna, Austria



There are still some places at the conference left. To register and find out more, visit: www.oncoconferences.ch/bcc

The 16th St Gallen International Breast Cancer Conference will be held in Vienna, Austria, from 20-23 March this year. For many years now this prestigious conference, which attracts close to 3,000 delegates from all over the globe, has set the benchmark in primary therapy of early breast cancer. The conference is renowned for its quality and its leading international speakers, who represent the best in breast cancer research and therapy worldwide. The highlight of the congress is the St Gallen Breast Cancer Consensus conference on Saturday, in which up to 60 experts gather on stage to engage in a live-voting process on therapy of early breast cancer. This shapes treatment procedures for the coming two years. Participants are sure to witness history in the making for the good of breast cancer patients worldwide.

The Swiss-based Foundation St Gallen Oncology Conferences (SONK) is the official organiser. The organising and scientific committees involve experts from St Gallen and Vienna, and also from countries including Italy, Belgium and the USA. Attendees are expected from around 100 countries.

The conference, which is being held in Vienna for the third time, combines the best of Swiss

precision and thoroughness with the strengths of Vienna as a destination: a centrally located meeting place of cultures, which attracts researchers and clinicians from all over the world. In addition, Vienna is a treasure trove of culture and history. Whether it's music, architecture or cuisine, there will not be a dull moment during congress hours or after.

The event is supported by an industry exhibition, showcasing the latest technology for breast cancer diagnosis and care. Industry will also have the opportunity to hold their own activities for attendees.

The closing date for abstracts was mid-December 2018. All accepted abstracts will be displayed as posters in a designated poster exhibition, the best of which will receive awards.

The conference is pending formal accreditation, which is expected to be around 18 continuing medical education (CME) credits.



Predictive models in external beam radiotherapy

25-27 March 2019
Naples, Italy

To find out more, visit:
www.fisicamedica.it

The fourth edition of the ‘Predictive models in external beam radiotherapy’ course will be held in the amazing city of Naples, Italy, from 25 to 27 March 2019. This international course is organised by the Italian Association of Medical Physics (AIFM) (www.fisicamedica.it).

The aim of the course is to bring participants up to date with all the most important news in predictive modelling in radiotherapy, and to provide an overview of state-of-the-art modelling approaches.

Experts in the field will provide comprehensive contributions on personalisation of treatment, improvements in knowledge on dose-volume relationships for different organs, including an update of the quantitative research data available. In addition, new and important issues will be addressed. These include pre-clinical research on animal models, voxel-based approaches to analysis of radiation-induced toxicity and treatment failure and survival, the integration of clinical/genetic/imaging parameters in prediction models, and the application of predictive models in planning and adaptive radiotherapy. Finally, we will discuss needs and modalities for data sharing in outcome modelling.

As well as exploring these advanced topics, the course also covers material related to the basics of radiology applied to radiotherapy and ‘traditional’ normal tissue complication probability (NTCP) and tumour control probability (TCP) models.

The course is aimed at all radiation oncology professionals who want to acquire a comprehensive overview of these modelling issues, in terms of both knowledge and methodology. This includes radiation oncologists, medical physicists, data scientists and clinical/pre-clinical researchers.

The 14th International Netherlands Cancer Institute Head and Neck Symposium
Diagnosis and treatment of head and neck cancer: locally advanced tumours

4-5 April 2019
Amsterdam, The Netherlands



Since 1993, the Netherlands Cancer Institute has held 13 successful multidisciplinary symposia on the diagnosis and treatment of a variety of malignancies in the head and neck. Each symposium attracted an audience consisting of a large number of highly interested national and international specialists, actively participating in discussions.

The forthcoming 14th symposium is focused on the diagnosis and treatment of locally advanced tumours. Many recent developments, such as continuing epidemiological research, new insights in molecular biology, more understanding of the role of HPV, advances in 3D technology and the breakthrough of immunotherapy, have changed the approach to head and neck cancer treatment dramatically. These innovations may not only improve the outcome, but also pose new challenges for multidisciplinary tumour boards in appropriate decision-making.

The forthcoming symposium will highlight the pitfalls in implementation of these recent achievements in daily clinical practice. Lectures by keynote speakers will bring you up to date on general knowledge and we will discuss case reports in relation to the implementation of the acquired knowledge.

The symposium is relevant to both residents and specialists working in the field of otolaryngology head and neck surgery, oral and maxillofacial surgery, medical oncology, general surgery, radiotherapy, pathology, dermatology, radiology, speech and language pathology, fellows and residents in training. Lectures and presentations will introduce you to the latest advances and state-of-the-art diagnosis and treatment of head and neck cancer, and will feature time for discussion. The range of speakers represent the multidisciplinary character of this symposium.

The symposium is open for poster presentations dealing with controversies and multidisciplinary management in locally advanced head and neck tumours. During the coffee break in the afternoon on 4 April a 'poster tour' will be organised and all participants are urged to view the posters. Faculty members will facilitate and take part in the discussions with attendees at the posters.

To find out more, visit: www.hoofdhalskanker.info/symposium-head-and-neck-cancer

ESHO 2019: 33rd annual meeting of the European Society for Hyperthermic Oncology (ESHO)

22–24 May 2019
Warsaw, Poland



To find out more, visit:
www.esho.info/congresses.html

Hyperthermia or thermal therapy is the heating of tumour tissues to temperatures ranging between 40 and 44°C. For many years hyperthermia has been known as a very effective sensitiser for radiotherapy and chemotherapy. Recent radiobiological research revealed the pathways along which hyperthermia affects DNA repair and hence sensitises tumour cells for DNA damaging agents. The clear benefit of combining radiotherapy/chemotherapy with hyperthermia has been demonstrated in an abundant number of prospective and randomised clinical trials, showing both increased local control and survival. In addition, thermal dose effect relationships have been demonstrated and are inspiring further innovation in hyperthermia technology.

All scientists and clinicians active in the biological, technological or clinical research aspects of hyperthermia are represented by ESHO, coming together at the annual meeting to exchange the latest scientific progress. A key aspect of the ESHO annual meeting is that it facilitates in-depth discussions, exchange of knowledge and good social meetings between friends and colleagues working in hyperthermia in an excellent environment.

You are invited to participate in the 33rd annual meeting of the ESHO, which takes place in Warsaw, Poland, from 22 to 24 May 2019 (www.esho2019.eu). Endorsed by ESTRO, the event has the ambition of putting a new milestone in the development of hyperthermia by offering an optimal meeting space for researchers, clinicians, physicist and engineers. All participants are encouraged to cross their disciplinary frontiers in order to exchange views and experiences.

The meeting offers an exciting programme, which starts with an educational day. The meeting then continues with clinical hot topics. The synergies between hyperthermia and radiotherapy, chemotherapy and immune-stimulating drugs have been explored for several decades. New discoveries encourage us to keep searching. Let us meet and talk in the capital of Poland, which is rich both in culture and history, and full of young and fresh energy.

Professor Gerard C van Rhoon
ESHO President



PAST CONFERENCE

**XVI Annual TMH Radiotherapy Practicums:
'Image-guided radiotherapy: a radiation therapist's perspective' ▶▶**

15-16 September 2018 | Mumbai, India

XVI Annual TMH Radiotherapy Practicums: 'Image-guided radiotherapy: a radiation therapist's perspective'

15-16 September 2018
Tata Memorial Centre
Mumbai, India



XVI Annual TMH Radiotherapy Practicum PICTURE

Radiation therapy aims to achieve an optimum balance between competing objectives of highest dose to the target volume and causing the least morbidity by respecting normal tissues. This has led to the landscape of modern radiation therapy, which is adopting advanced forms of intensity-modulated radiation therapy (IMRT), image-guided radiation therapy (IGRT), and 4D radiation therapy (4D-RT), employing imaging modalities ranging from simple planar imaging to several volumetric imaging modalities. This has been combined with the development of new and proven investigational devices adding to the

radiotherapy armamentarium. Highly specialist computers are fuelling parallel advances in imaging technologies, such as co-registration of multi-modality imaging techniques to ensure better visualisation of the anatomy and more accurate capturing of its motion.

The rapid pace of these developments is ushering in an era where radiation therapists (RTTs) are required to add new capabilities to their skillset in order to deliver the most effective radiotherapy workflow. It also demands more joint working with colleagues to establish consensus on the ▼



RAHUL KRISHNATRY



JAI PRAKASH
AGARWAL

implementation, appropriate documentation and the review process that accompanies the adoption of a new practice across an institution. It was against this background that the 'XVI Annual TMH Radiotherapy Practicum' was developed, with practicing RTTs from across India and south Asia coming together for hands-on training.

In total, there were 49 delegates from 47 institutes based in 32 cities across India, as well as two delegates from other countries in south Asia. All the participants were from radiotherapy centres that had, as a minimum, volumetric imaging-based IGRT systems. About half of the participants also had motion management techniques available at their centres. The faculty was made up of one national lecturer, one international lecturer (from ESTRO) and local faculty members.

The programme was delivered over two days, with lectures in the morning and practical hands-on demonstrations in the afternoon. The first day began with a lecture introducing IGRT and its workflow, and the role of the RTT. A range of IGRT strategies were discussed during the afternoon's practical session, and were demonstrated for common treatment sites in

India, including head and neck, cervical, prostate, bladder, lung, and breast cancer.

On the second day the lectures focused on motion management techniques. This included a detailed discussion of 4D-RT in lung cancer and deep inspiration breath-hold techniques (DIBH) for breast and abdominal malignancies. Following this, there was a brief introduction to quality assurance (QA) procedures related to IGRT equipment and technology from the RTT's perspective.

The Practicum generated a lot of enthusiasm among its participants, which was evident in the course feedback and the level of participation from the floor. It was also present in the enjoyable discussions that the participants had at the organised dinner. With ESTRO's continuing support, the course will go a long way towards developing the practice of RTTs across the region.

This course was the first hands-on training for RTTs in south Asia, and we are grateful for ESTRO's support. The organising committee thanks the Tata Memorial Centre directors, the course faculty, ESTRO and all the participants for making this an enriching experience. We hope that in the future there will be many

similar interactive education programmes for RTTs in India. This will help to develop modern radiotherapy practice in the region, ensuring that our RTTs deliver optimal treatment to the highest international standards.

Dr Rahul Krishnatry
Organising secretary

Professor (Dr) Jai Prakash Agarwal
Organising chairman

International Symposium on

Standards, Applications and Quality Assurance in Medical Radiation Dosimetry

18–21 June 2019 Vienna, Austria

Organized by the International Atomic Energy Agency

50

YEARS

1969 – 2019

of IAEA/WHO
Dosimetry Audits

IDOS 2019



IAEA

International Atomic Energy Agency

Atoms for Peace and Development



Bridging the Gap

Advanced Breast Cancer

Fifth ESO-ESMO International Consensus Conference

14-16 November 2019 | Lisbon, Portugal

Coordinating Chair: F. Cardoso, PT

Chairs: E.P. Winer, US - L. Norton, US - A. Costa, IT/CH

Co-Chairs: G. Curigliano, IT - S.A. Mertz, US

Scientific Committee Members: K. Gelmon, CA

F. Penault-Llorca, FR - E. Senkus, PL - C. Thomssen, DE

The ABC5 guidelines will be developed by ESO and ESMO



The ABC5 conference and guidelines are endorsed by



The ABC5 conference is held

under the auspices of



with official representatives of



and is endorsed by



RECEIVE UPDATES AT WWW.ABC-LISBON.ORG | #ABCLISBON



CALENDAR OF EVENTS



MARCH 2019

14-16 MARCH 2019 | BARCELONA, SPAIN

7th ICHNO

www.estro.org/congresses-meetings/items/7th-ichno



20-23 MARCH 2019 | VIENNA, AUSTRIA

The 16th St. Gallen International Breast Cancer Conference

www.oncoconferences.ch/bcc

ESTRO
ENDORSED EVENT

21-23 MARCH 2019 | SAN DIEGO, CA, USA

2019 RSS Annual Scientific Meeting

www.rssevents.org

ESTRO
ENDORSED EVENT

24-27 MARCH 2019 | NAPLES, ITALY

Predictive Models in External Beam Radiotherapy

www.fisicamedica.it

ESTRO
ENDORSED EVENT

APRIL 2019

4-5 APRIL 2019 | AMSTERDAM, THE NETHERLANDS

The 14th International Netherlands Cancer Institute Head and Neck Cancer Symposium

www.hoofdhalskanker.info/symposium-head-and-neck-cancer/

ESTRO
ENDORSED EVENT

9 APRIL 2019 | BRUSSELS, BELGIUM

5th European Particle Therapy Network (EPTN)

www.estro.org/congresses-meetings/items/5th-european-particle-therapy-network-eptn



26-30 APRIL 2019 | MILAN, ITALY

ESTRO 38

www.estro.org/congresses-meetings/items/estro-38



MAY 2019

15-17 MAY 2019 | FLORENCE, ITALY

Annual Meeting of the European Musculo Skeletal Oncology Society 2019

www.emsos2019.eu

ESTRO
ENDORSED EVENT



17-18 MAY 2019 | DUBLIN, IRELAND

Annual Irish Stereotactic Radiosurgery and Stereotactic Ablative Radiotherapy Symposium

<https://irishsrsandsbrtsymposium.com>

ESTRO
ENDORSED EVENT

22-24 MAY 2019 | WARSAW, POLAND

ESHO 2019

<http://esho2019.eu>

ESTRO
ENDORSED EVENT

JUNE 2019

18-21 JUNE 2019 | VIENNA, AUSTRIA

International Symposium on Standards, Applications and Quality Assurance in Medical Radiation Dosimetry (IDOS 2019)

www.iaea.org/events/idos2019

IN COLLABORATION
WITH ESTRO

19-22 JUNE 2019 | BANGKOK, THAILAND

PROS - Congress of the international paediatric radiation oncology society

intpros.org/congress/next-pros-congress

ESTRO
ENDORSED EVENT

19-22 JUNE 2019 | DUBROVNIK, CROATIA

ESOI Oncologic Imaging Course 2019 - Oncologic Imaging in the era of precision medicine: Challenges and opportunities

www.esoi-society.org/index

ESTRO
ENDORSED EVENT

AUGUST 2019

1-2 AUGUST 2019 | TEHRAN, IRAN

3rd International Conference on Head and Neck Cancer

ESTRO
ENDORSED EVENT

29-31 AUGUST 2019 | BASEL, SWITZERLAND

Advanced Prostate Cancer Consensus Conference (APCCC) 2019

www.apccc.org/apccc2019.html

ESTRO
ENDORSED EVENT



SEPTEMBER 2019

09-11 SEPTEMBER 2019 | PARIS, FRANCE

**Association of systemic treatments and radiation therapy in breast cancer:
From evidence based to clinical practice**

ESTRO
ENDORSED EVENT

OCTOBER 2019

25-26 OCTOBER 2019 | VENUE TO BE ANNOUNCED

3rd ESTRO Physics Workshop - Science in Development

www.estro.org/congresses-meetings/items/3rd-estro-physics-workshop

 ESTRO EVENT

NOVEMBER 2019

14-16 NOVEMBER 2019 | LISBON, PORTUGAL

ABC5

www.abc-lisbon.org

ESTRO
ENDORSED EVENT

21-22 NOVEMBER 2019 | BUDAPEST, HUNGARY

7th GEC-ESTRO workshop

www.estro.org/congresses-meetings/items/7th-gec-estro-workshop

 ESTRO EVENT

DECEMBER 2019

6-8 DECEMBER | SINGAPORE

ESTRO meets Asia

 ESTRO EVENT

MARCH 2020

30 MARCH - 1 APRIL 2020 | CAMBRIDGE, UK

The role of Epigenetics in DNA Damage Response, DNA Repair and Radiosensitivity

www.eacr.org/conference-series

IN COLLABORATION
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ESTRO

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