SOCIETY LIFE
HERO project: three first papers published. How will it impact the future practice of radiotherapy in Europe?

PROJECTS & RESEARCH
Union of Light Ion Centres in Europe (ULICE): final meeting report

ESTRO SCHOOL
ESTRO Fellow 2015: what to expect? Interview with Fiona Stewart

RADIOBIOLOGY
Special focus on DNA repair

NEWSLETTER NOVEMBER - DECEMBER
ESTRO | EUROPEAN SOCIETY FOR RADIOTHERAPY & ONCOLOGY

Nº 97 | BIMONTHLY | NOVEMBER - DECEMBER 2014
<table>
<thead>
<tr>
<th>CONTENTS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Editorial</td>
<td>3</td>
</tr>
<tr>
<td>Society Life</td>
<td>6</td>
</tr>
<tr>
<td>Clinical</td>
<td>20</td>
</tr>
<tr>
<td>Read it before your patients</td>
<td>26</td>
</tr>
<tr>
<td>Brachytherapy</td>
<td>42</td>
</tr>
<tr>
<td>Physics</td>
<td>51</td>
</tr>
<tr>
<td>RTT</td>
<td>61</td>
</tr>
<tr>
<td>Radiobiology</td>
<td>74</td>
</tr>
<tr>
<td>ESTRO School</td>
<td>87</td>
</tr>
<tr>
<td>Young ESTRO</td>
<td>110</td>
</tr>
<tr>
<td>Health Economics</td>
<td>122</td>
</tr>
<tr>
<td>Projects &amp; Research</td>
<td>126</td>
</tr>
<tr>
<td>Institutional Membership</td>
<td>130</td>
</tr>
<tr>
<td>ESTRO Conferences</td>
<td>134</td>
</tr>
<tr>
<td>Calendar of events</td>
<td>150</td>
</tr>
</tbody>
</table>
“The report in the following pages shows how collecting data on equipment, guidelines and staffing is mandatory to advocate for radiotherapy in the public health arena”

Dear friends and colleagues,

Autumn is well on its way and without having the time to realise it, Christmas will soon be knocking on the door.

The ESTRO Board has continued to work on the decisions taken at the June strategy review (JSR) meeting. There is still a lot of work to be done and it will continue for several months on all governance levels of ESTRO. We will be able to present you with the outcomes of all the discussions and decisions important for the future of the Society in an upcoming issue of the Green Journal.

However, I can already tell you that it was agreed that for the development of our Society international collaborations are vital. Our collaboration with the Canadian Association of Radiation Oncology (CARO) is such an example. You can ▼
read a report on the CARO annual congress in the Clinical Corner with a focus on the ESTRO-CARO session. In the Society Life Corner we are happy to announce that a new Memorandum of Understanding (MoU) has been signed between our two societies.

Also in the Society Life Corner, do not miss the report on the Health Economics in Radiation Oncology (HERO) project. Initiated in 2010, the project has now published its first three articles. The report in the following pages shows how collecting data on equipment, guidelines and staffing is mandatory to advocate for radiation oncology in the public health arena.

On top of working hard on the governance level of the Society, there has been continued work on the preparations for the 3rd ESTRO Forum. Registration is now open so we encourage you to register at the early fee rate by 20 November 2014. In addition to a terrific scientific programme, next year the Forum will welcome for the first time a job fair where companies and institutes at dedicated booths will gladly receive candidates to discuss potential career opportunities. There is no other venue than the ESTRO congress to gather simultaneously such highly specific candidates and employers. Alessandro Cortese, ESTRO’s CEO will tell us more in the Conference Corner about the reasons why ESTRO can facilitate the job market place in radiation oncology. We hope you will take this opportunity to further your career.

Enjoy the end of the year with all its festivities and I look forward to being in touch again in early 2015.

Philip Poortmans
ESTRO President
SOCIETY LIFE
It gives me great pleasure to introduce the report on the first work package of the ESTRO Health Economics in Radiation Oncology (HERO) project. The HERO project started four years ago and the first three papers were recently published in the Green Journal. In this corner, the leaders of the HERO project comment on the results of their studies and provide us with a new perspective on the data collected throughout Europe on guidelines, equipment and staffing.

In our daily practice, we are continuously confronted with the need to make right choices in order to make the most effective use of resources. In this context, the importance of a project such as HERO becomes obvious.

But beyond the data displayed in these three studies, the comments from the experts, both from radiation oncology and health economics, teaches us a lot about the practice of radiation oncology in Europe. ESTRO has been making efforts ceaselessly to ensure radiation oncology is recognised as a cost effective treatment for cancer in the public health arena. Now with the first HERO work package finished, I am convinced that we are moving in the right direction.

Philip Poortmans
ESTRO President

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ESTRO EXTRAORDINARY GENERAL ASSEMBLY - 16 DECEMBER 2014

ESTRO Budget for 2015 to be approved

An Extraordinary General Assembly (EGA) will be held on 16 December, 18:30-19:00 CET at the ESTRO office. It will also be possible to join the EGA virtually via WebEx. The EGA has been called to approve the ESTRO budget for 2015. The official invitation with the confirmed agenda, material and the login details will be sent in accordance with the statutes to all ESTRO full members in good standing order in due time.
After starting four years ago, the Health Economics in Radiation Oncology (HERO) project, initiated by ESTRO, has recently completed its first work package. Three papers describing the progress made on the HERO project have just been published in the October issue of the Green Journal. In the following pages, we highlight, with the help of the Chairs of the project, why HERO, and more importantly these first results, are essential for the future practice and development of radiotherapy in Europe.

Why developing a cost effective model in radiotherapy is a necessity?

The sustainability of quality healthcare in an increasingly resource constrained environment is an ongoing challenge. Central to the healthcare funding debate is the need to demonstrate cost effectiveness and value. With the rapid evolution in radiotherapy, made possible with new sophisticated technologies and highly specialised and trained staff, quantifying costs and benefits is complex.

Against this background, the ESTRO HERO project aims at developing a knowledge base and a model for health economic evaluation of radiation oncology at the European level. The project addresses the following key factors: needs, provision and accessibility of radiotherapy, cost-accounting and economic evaluation. Through the collection, validation and analysis of the relevant data, the HERO project will be used to advocate for radiotherapy to European governments and other healthcare stakeholders whose decisions ultimately affect the care of patients.

Initiated in 2010 with a kick-off meeting at ESTRO 29 in Barcelona, the HERO project became a major activity within ESTRO and is an integral part of the ESTRO vision for 2020:

“ESTRO will further support the development of innovative health services research in radiotherapy and oncology, including the long term analysis of changes in specialist staffing in the discipline, the level of equipment, the appropriate implementation of new technology, patient access to new treatment approaches; together with the critical analysis of these strategic developments using cost-benefit, cost utility and other means of health economic review and health technology assessment (HTA). In the first instance ESTRO has initiated this strategic priority through the creation of the HERO project”.

It is rewarding now to see that the efforts of the HERO group and their collaborators in the national societies are bearing fruit. Looking forward to 2020, the HERO project will provide the European radiotherapy community with valuable outcomes and tools to assist national societies and institutions in their daily management, planning and prioritisation.
Finally, in demonstrating the cost effectiveness of radiation oncology, HERO supports ESTRO in its mission to promote radiotherapy within Europe and beyond.

**HERO GROUP**  
**FIRST WORK PACKAGE**  
- Cai Grau (Chair), Radiation Oncologist, Aarhus University Hospital, Aarhus (Denmark)  
- Yolande Lievens (Chair), Radiation Oncologist, Ghent University Hospital, Ghent (Belgium)  
- Marta Bogusz-Czerniewicz, Radiation Oncologist, Cancer Diagnosis and Treatment Center, Katowice (Poland)  
- Josep Borras, Epidemiologist, Catalan Cancer Strategy, L’Hospiitalet de Llobregat, Barcelona (Spain)  
- Mary Coffey, Radiation Therapist, School of Medicine, Trinity College Dublin, Dublin (Ireland)  
- Noémie Defourny, Health economist, ESTRO Office, Brussels (Belgium)  
- Peter Dunscombe, Medical Physicist, University of Calgary, Calgary, Alberta (Canada)  
- Chiara Gasparotto, Public Affairs Manager, ESTRO Office, Brussels (Belgium)  
- Julian Malicki, Medical Physicist, Great Poland Cancer Centre, Poznan (Poland)  
- Ben Slotman, Radiation Oncologist, VU University Medical Centre, Amsterdam (The Netherlands)

**Work package 1: aimed to get a clear picture of the European resources**

The first work package of the HERO project is now complete with three papers recently published in the Green Journal (issue 112, volume 2). Work package one sets the scene by providing an overview of European radiotherapy based on a survey of resource availability (departments, equipment and personnel) and guidelines.

The three papers report the final results on:
- Radiotherapy equipment and departments in the European countries
- Radiotherapy staffing in the European countries
- Guidelines for equipment and staffing of radiotherapy facilities in the European countries.

**COLLECTION OF DATA**

A web-based questionnaire consisting of 84 questions relating to population and cancer incidence, radiotherapy courses and resources, guidelines and reimbursement was developed and distributed to national scientific and professional radiotherapy societies of European countries. The data collected through this exercise were checked and cleaned for methodology harmonisation.

Data on radiotherapy reimbursement have also been collected in the ESTRO-HERO survey and will be analysed at a later stage.

**THE INVOLVEMENT OF NATIONAL SOCIETIES**

The national societies have played a central role in the first work package and in populating the HERO database. The start of a project with a scope as broad as HERO’s is probably the slowest, yet the most essential part as it requires agreement on a robust methodology, data acquisition, data cleansing, data validation and surmounting the inevitable obstacles encountered along the way.

The HERO group was fortunate in being able to rely on not only its internal expertise but also on the ever fruitful collaboration and exchange with the European national societies. The collection of data was a difficult step and could not have been accomplished without the national societies’ delegates devoting much of their precious time to this aspect of the project. Through this updated and validated description of European radiotherapy resources, ESTRO is providing the basis for European countries and their radiotherapy societies to advocate for radiotherapy at a national level and, in subsequent phases of the HERO project, to compute the cost and cost effectiveness of radiotherapy in specific national economic contexts. ▼
## WORK PACKAGE 1
### Availability and actual state of European radiotherapy

**Aim:** to obtain an overview of radiotherapy in Europe, giving a clear picture of equipment, staffing, guidelines and reimbursement currently available.

**Method:** ESTRO-HERO survey

### Table

<table>
<thead>
<tr>
<th>Topics</th>
<th>Deliverables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics, cancer incidence and radiotherapy utilisation</td>
<td>Validated and cleaned data set, per country</td>
</tr>
<tr>
<td>Infrastructure, equipment and staffing</td>
<td>Key parameters relating resources to cancer incidence, radiotherapy utilisation, population density and gross national income, by country</td>
</tr>
<tr>
<td>Guidelines on radiotherapy resources</td>
<td>Analysis of the guidelines on radiotherapy resources, comparison to QUARTS* and worldwide guidelines</td>
</tr>
<tr>
<td>Reimbursement</td>
<td>Reimbursement paper to be planned at a later stage, along with the development of the costing model</td>
</tr>
</tbody>
</table>

*QUARTS: quantification of radiotherapy infrastructure and staffing needs

### Overview of the countries participating to HERO

- submitted data for the three articles
- submitted data for two articles out of three
- submitted data for one article out of three
- no submission of compliant data
First set of results: What do we learn about radiotherapy practice throughout Europe?

Interview with the leaders of the HERO-project

Yolande Lievens and Cai Grau, Chairpersons of the HERO project, and Peter Dunscombe, who was responsible for the guideline paper, shed some light on the large data set collected and the interpretation of this first series of results.

A) EQUIPMENT

Interview with Cai Grau, co-Chair of the project Aarhus University Hospital, Aarhus, Denmark

In the three papers, a common theme is the variability across Europe. Can you briefly elaborate on the variability your data demonstrate?

The richness and the beauty of Europe lies in its diversity. When we embarked on this project, we knew very well that differences and variability would be key and recurring themes in our long discussions.

Indeed, there is a huge variation in the availability and sophistication of treatment equipment and staffing levels across Europe. Just to give you a flavour of the variation we found across the European radiotherapy panorama, and you can find more details in the three papers, there is a seven-fold variation in MV units per million inhabitants and a twenty-fold variation for staffing, after grouping personnel with comparable duties in the radiotherapy process. Regarding guidelines, the majority of the respondent countries do have guidelines, but often with very different denominators. For example, inhabitants, patients, and fractions, have all been reported as the metric used to calculate the number of linear accelerators (LINACs) required in a country.

Why is it necessary to investigate and describe the variation of RT in Europe?

Highlighting the variability in the use of radiotherapy throughout Europe with reliable data is just the first step. In cancer care, the variability of factors such as demographics, cancer incidence and survival, wealth, available resources, service delivery models and funding, all need to be considered when planning optimal radiotherapy resources to meet patients’ present and future needs. And this is what the whole HERO project is aiming at: the provision of the tools and information which the radiotherapy community needs in order to advocate for radiotherapy with the various stakeholders who take strategic decisions concerning radiotherapy provision.

As you just told us, describing the European radiotherapy panorama is not an easy task, due in part to its diversity. Looking back now, having published the first papers, what were the main challenges that you encountered during this first phase of the HERO project?

For the moment, we have a nice fulfilling sense of accomplishment with our first publications, though, if I look back at the past few years, the challenges we encountered were many. Addressing these challenges took very long and complex exchanges and debates within the group resulting in some simplifications in the methodology employed. These simplifications were inevitably accompanied by limitations in the study which we also discussed in detail to make sure they were acceptable within the broad context of our endeavour.

The first challenge was to put together a questionnaire that was comprehensive, encompassing national differences but, at the same time, being clear and self-explanatory. Not an easy task, I can assure you.

Next was the data collection itself. As we’ve already mentioned the active support of national societies and professional organisations was absolutely essential during this phase of the study. We are grateful for the effort that all national societies collaborators made, especially as we do realise that much of the requested data were not readily available at country level and had to be collected nationwide first. However, inevitably, there were many follow-up phone calls and emails to resolve discrepancies and seek clarifications related to the data submitted.

...
For example, while focusing on the robustness of the data as our key priority, we recognised that the data available to national societies pertained to different years. This limitation is acknowledged in the discussions of the data. How difficult was it to interpret such diverse data?

It is very important to point out that there can be biases in the interpretation of the questions and also of the replies. As mentioned before, Europe means variability and complexity, and often it is not possible to summarise complexity with a number, or with a single line reply. So, yes, interpretation of the mass of data accumulated during the study absorbed a large amount of effort. Another major point, that has been highlighted by the national societies during their annual meetings, and that we have discussed in the three papers, is that national averages disregard regional variations such as population density, cancer incidence, accessibility to care, regional health care and reimbursement systems. For some countries this is very important and must be taken into consideration when reading the HERO data critically.

Histogram showing the average number of radiotherapy courses per radiation oncologists (blue), medical physicists and dosimetrists (green), nurses and radiation therapists (orange) in the HERO countries.
Technology is evolving rapidly and hence the data published today – especially about equipment – will be outdated in just a few years.

The project relies a lot on the national societies. What has been their role?
The national societies have been our most important ally. Without them the study would not have been possible. Many of the national societies’ representatives faced significant challenges such as when no national database existed in which case they had to start data gathering from scratch.

B) GUIDELINES
Interview with Peter Dunscombe, University of Calgary, Calgary, Alberta, Canada.
Lead of the HERO paper: Guidelines for equipment and staffing of radiotherapy facilities in the European countries: final results of the ESTRO-HERO survey

One of the three studies released focuses on guidelines and reveals that guidelines do not always keep pace with practice. How should the radiotherapy community solve this issue?
Before answering that question it is worth pointing out that many countries have developed guidelines for equipment and staff inventories although, as your question suggests, they are not necessarily current in our rapidly changing environment. If we compare the results presented in the guidelines paper with those in the staffing and equipment ones, the process of guideline updating is slower than changes in practice. The field of radiotherapy is a rapidly evolving one, largely due to technological developments allowing novel radiotherapy approaches (e.g. evolution towards hypofractionation, introduction of adaptive radiotherapy, motion management) and new schemes of chemoradiation. To accommodate these changes guidelines should be under constant review. Adopting clear and logical metrics for staffing and equipment inventories would definitely help as would harnessing modern communication technologies for the updating and dissemination of guidelines.

Does it mean that our current guidelines are not reliable?
Current guidelines can be regarded as a starting point but it has to be recognised that most of them were developed when our lives and the tools we had at our disposal were much simpler. Guidelines of the future will need to be structured to accommodate changing roles and technology, clinical practice and operational issues.

These data will evolve with time. Are updates foreseen?
We are confident now that the system is in place, further updates could be collected efficiently in the future. With an improved version of the questionnaire, and the experience acquired by the HERO group and the national societies representatives, it will be relatively straightforward to maintain the current database.
How can the first HERO results have an impact on guidelines?

We’ve learnt several things from this exercise. It’s clear that the majority of guidelines do not reflect today’s reality. So staffing and equipment purchasing decisions must be made at least partly on an ad hoc basis. Further, many of the guidelines available are not necessarily structured in a way that facilitates decision making. Guidelines should ideally not only describe the reality, but also guide the introduction of new facilities or the upgrade of current facilities ensuring both safety and quality while, at the same time, avoiding waste through unnecessary duplication and inefficient use of limited resources, especially during these hard times. This component of the HERO project has highlighted the challenges of guideline development in changing times and will hopefully lead to innovative ways of rising to this challenge.

How do you envision the guidelines of tomorrow?

Looking to the future, realistic health economic models, populated with accurate demographic and epidemiological information projected into the future, would be sensible bases for guideline development. Such an approach would provide us with not just a description of the current situation but also a forecasting tool, helping us to reassess and rethink our reimbursement and operational models. Clearly there are challenges ahead. However, we believe that HERO is leading the way towards addressing these challenges.

C) STAFFING

Interview with Yolande Lievens, co-Chair of HERO
Ghent University Hospital, Ghent, Belgium

Does the study show major differences from one country to another in terms of staffing? How different are the roles of the various disciplines of radiotherapy?

Indeed, professionals in different countries may have very different roles and responsibilities. Staffing is surely a national issue, linked to the history and education system of the country.
Tasks that in some countries are covered by one professional group might be covered by some other professional group in another country. Hence, tasks may differ quite substantially from country to country, and even within countries. For example, the radiation therapists (RTTs) tasks in Europe, range from being limited to treatment delivery to taking up a large part of the preparatory phase including planning, research and development, patient information and support. Another striking example is the role of the dosimetrists, a profession that doesn’t exist in some countries.

Apart from having different tasks, the involvement of each professional in the radiotherapy process varies as well: the participation of physicists in treatment planning and quality assurance procedures might be covered by other professionals, with responsibility shared equally between radiation therapists, dosimetrists and/or physicists in high resource countries but with a predominance of the latter in low resource countries. Or, again, the time a radiation oncologist devotes to administering chemotherapy is very different across Europe, influencing staff requirements. There are many variables which complicate the puzzle.

How did you proceed to get the overall picture of the different disciplines of radiotherapy?
To overcome this complexity, we tried to group selected categories of professionals who can perform similar jobs in Europe. However, even combining radiation therapists with nurses and medical physicists with dosimetrists, there was still huge variability in staffing levels across Europe.

At the level of the collection of staffing data, both actual numbers and full time equivalents (FTE) were requested from the national societies. The FTE were not always available or not robust, therefore we decided to use the actual number, though including in some cases the FTE, if those were the only available data. This issue is further clarified in the staffing paper. Another important factor is educational activities performed by the staff, and how to account for trainees in our analysis. The issue of accounting for time ▼
dedicated to education and research should be investigated further.

Who could benefit of the release of these data in staffing?
We believe that providing such comparative data will strengthen the European national societies in their discussions with governments and financing agencies and will help them to reduce any shortfall in radiotherapy staff by developing educational programmes that strive to better align the actual resources to the needs. As discussed below, the calculation of the needs is the next step being undertaken within the HERO project.

What are the next steps for the HERO group?
The future is very exciting for the HERO group. The forthcoming step, with work package number two led by Josep Borras, is an epidemiological assessment of the impact of variations in cancer incidence and stage at diagnosis on the optimal utilisation rate. Our starting point is the study presented by the Australian CCORE group (Collaboration for Cancer Outcomes, Research and Evaluation). Decision trees have been designed for each tumour site, linking literature evidence supporting radiotherapy by site to detailed incidence data by site and stage. As such the optimal proportion of patients who should receive radiotherapy is determined.

How can HERO apply the Australian model to the European one?
The HERO group “translates”, if we can say so, the Australian trees to the European reality. The work is in progress. European data on cancer incidence by site and stage at diagnosis were needed in order to fill in the decision trees. The data on the stage at diagnosis are not so easy to obtain but four cancer registries were able to provide those data according to the

![Number of courses per medical physicist and dosimetrist](image-url)
specifications of the CCORE decision trees (Belgium, The Netherlands, Great Poland region from Poland and Slovenia). We hope we will soon be able to present the results in the next HERO papers.

**HERO also plans to develop a costing model. What are the benefits for the radiotherapy community of such a model?**

The model will be a really useful tool for the national societies and for the radiotherapy community, allowing them to identify how the allocation of resources translates into radiotherapy costs at the national level and treatment. Moreover, it will help in forecasting staffing and equipment needs into the future. The costing model is based on the Time Driven Activity Based Costing methodology (TD ABC), and will be tailored to radiotherapy and applicable at country level. We are now defining the variables of the model.

**How can a costing model impact on the management of cancer?**

We believe that having a costing model, specific for radiotherapy, will be useful not only as an instrument to manage radiotherapy resources and their cost, but also as a basis for proving value for money of radiotherapy. In time, this will help us to advocate for radiotherapy and ultimately for the multidisciplinary management of cancer.

**Note for figure:**

**Number of courses per radiation therapists (RTT) and radiotherapy nurses**

1. Dotted lines are the ranges when provided by countries.
2. Only countries having data from at least two of the three data sources are shown.
3. HERO and QUARTS guideline data have been adjusted for a 25% re-treatment rate whenever the guideline stated explicitly new patients.

**INTERESTED IN PUBLIC HEALTH ISSUES?**

Don’t miss the Health Economics Corner. This issue, an article on “Should we continuously update the evidence?”

Read the article on p 124 >
MEMORANDUM OF UNDERSTANDING

Between the Canadian Association of Radiation Oncology (CARO) and ESTRO

The Canadian Association of Radiation Oncology (CARO) and ESTRO have been collaborating fruitfully for years on joint symposia and society membership. On 27 August 2014 both societies signed a renewal of the Memorandum of Understanding (MoU) at the annual scientific meeting of CARO at Saint John, Newfoundland, Canada. They thereby confirmed that they would continue this valued collaboration for the years to come.

CARO President Dr Ross Halperin said: “On behalf of CARO, I am thrilled to continue this valued collaboration with ESTRO in the field of radiation oncology. CARO members benefit greatly by being part of the ESTRO family and in turn we hope that CARO contributions serve to enrich ESTRO.”

ESTRO President Professor Philip Poortmans said: “I am very happy with this confirmation of our collaboration in the field of radiation oncology that will lead to a clear win-win outcome for both societies.”

The MoU is valid until the end of 2020 and covers themes including joint symposia, society membership and the publication of abstracts from the CARO annual scientific meeting in the ESTRO journal *Radiotherapy and Oncology (Green Journal)*. A joint ESTRO-CARO symposium will be held each year; the symposium will take place at ESTRO and CARO congresses in odd and even numbered years, respectively. Other joint fields of interest were discussed that can be set up jointly.
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2015 MEMBERSHIP AVAILABLE ON WWW.ESTRO.ORG
Dear colleagues,

In this edition of the Clinical Corner, I am happy to share a report on the 2014 annual scientific meeting of the Canadian Association of Radiation Oncology (CARO). As you will see from the report a range of highly interesting and relevant topics were addressed. For example, hot topics in breast cancer such as Accelerated Partial Breast Irradiation (APBI) and regional treatment were discussed with different perspectives and experiences reported. Of note, in the ESTRO CARO joint session the European perspective was presented by our ESTRO President Professor Philip Poortmans who reported on the current evidence for regional radiation therapy in breast cancer.

Daniel Zips
This year’s annual scientific meeting (ASM) in Saint John Newfoundland and Labrador provided beautiful coastal scenery, scrumptious seafood and charming hospitality. The social events, including the resident pub trivia night and family scavenger hunt, reflected this city’s vibrant local culture, but are only part of the reason why such a wide range of attendees came to “the rock” for this year’s ASM.

From oncologists and physicists to radiation therapists and industry sponsors, the diverse audience of this year’s ASM reflected the varied interests of the Canadian Association of Radiation Oncology (CARO). Interest in the field is being cultivated through CARO, as exemplified through presentations from pre-medical and medical undergraduate students. Much of this work is fostered by the CARO-Canadian Radiation Oncology Foundation (CROF) summer studentship programme, which proudly announced another year of observerships awarded to medical students across the country. The CARO ASM refresher course is updated each year, providing an invaluable review of basic clinical knowledge to those either in training or brushing up on the latest evidence-based approaches.

Presenting more than standard clinical topics, the ASM highlights unique themes such as this year’s “Outcomes: clinical and professional” with opening lectures covering relevant and timely issues. Dr Manuel Borod explored end of life care issues with perspectives gleaned from his palliative care practice and with reference to Canadian law on euthanasia. Radiation oncologists often find

CLINICAL

CARO’S 2014 ANNUAL SCIENTIFIC MEETING IN REVIEW

28th CARO Annual Scientific Meeting

25 - 28 August 2014
Saint John, Newfoundland, Canada

ROSS HALPERIN
AMANDA CAISSIE
themselves supporting patients at the end of life and many of the issues raised by Dr Borod were commonly relevant to radiation oncology practice and the challenges these raise for many of us that we face routinely, yet are far from routine. Next Dr Derek Puddester picked up upon that theme and explored how these every day practice issues challenge physicians’ ability to cope on a personal level. He had us reflect and also challenged us to take care of our own psychological health.

Conference sessions represented the broad range of research and clinical expertise from Canadian oncology centres coast to coast, reflecting achievements at a local level, such as the benefits of telemedicine to assist remote regions. Other research studies emphasised the power of provincial databases to monitor essential patient outcomes. This conference was not, however, limited to a national scope. International speakers hailed from countries ranging from the US to Germany. Reporting on the establishment of an International Cancer Expert Corps (ICEC), Dr Norman Coleman provided the perspective of international collaboration and how it may assist with promotion of oncology care in developing countries.

The 2014 CARO lecture was given by Dr Paul Harari who spoke about head and neck malignancies and demystified the biological journey uncovered in head and neck malignancies. Dr Harari showed surprising data that challenged us to be careful of assumptions of efficacy through the story of cetuximab and chemoradiotherapy.

Dr Harari also joined CARO members for the annual CROF fun run and walk, on a beautiful morning by Saint John Harbour, a route which took runners a stone’s throw from where Terry Fox’s marathon of hope began. Those who participated in the CROF fundraising event were afforded not only pride in raising money for a good cause but also a pair of home-made Newfoundland knit socks for those in first place.

Dr Charles Hayter gave the Gordon Richards Lecture and tied in Canadian radiation oncology history to a view of radiation oncology through the arts. He explored what the lay public sees and thinks with regards to radiation oncology and the team delivering care. In so doing, Dr Hayter raised a call for concern for the future of our discipline. Radiation oncology provides a valuable public service and its current public image may be counterproductive to the public, health care professionals outside of radiation oncology and to governments.

The 2014 Jean Roy lecture was given by Dr Douglas Arthur, who presented a candid look at Accelerated Partial Breast Radiotherapy/Brachytherapy (APBI) and breast brachytherapy in the United States. His lecture spoke the supporting evidence for brachytherapy and the setting of American health care industry and it seemed the latter is at times a strong force directing care patterns in the USA. Growing use of 3.5 week fractionation schemes for breast cancer and evolving business incentive patterns have led to slowing of the →
growth of APBI. If there’s a future for brachytherapy APBI, Dr Arthur hypothesised that convenience, cosmetic outcome and local control will be the driving factors.

The meeting featured another CARO ESTRO symposium, which focused on radiotherapy for breast cancer. Dr Ivo Olivotto explored the evidence around APBI and gave an in-depth assessment of the RAPID trial outcome which showed that APBI given by external beam radiotherapy was not conformal enough to avoid cosmetic outcome disadvantage. Dr Olivotto suggested that brachytherapy may be an alternative APBI approach, however, data from large randomised trials will help answer that question. He also hypothesised from results from other APBI techniques that there are a subset of patients who might be able to avoid breast radiotherapy if their risk of recurrence is low enough and they are on a hormonal therapy such as tamoxifen. ESTRO President, Professor Philip Poortmans, explored regional radiotherapy for breast cancer, through an in-depth assessment of evidence; he gave the audience insights into who benefits from radiotherapy given to the nodes. He presented provocative data on the benefit of irradiating the internal mammary nodes, and in presenting the outcome differences in left and right IM radiotherapy, reminded us of the benefit of local control and the risk associated with normal tissue irradiation. These two complimentary presentations gave an in depth perspective of breast radiotherapy that was appreciated by those in attendance.

CARO remains committed to the promotion of opportunities for further radiation oncology education, through announcement of a fellowship in 2014 and another one planned for 2015. This year’s award ceremony introduced several new categories to recognise the diverse academic accomplishments across the field, including an award designated for fellows, survivorship research and best conference poster submitted to CUREUS, CARO’s online journal launched this year.

The most invaluable aspect of each CARO ASM may be the collaborations forged and relationships renewed. CARO promotes involvement in national initiatives such as the Canadian Partnership for Quality Radiotherapy (CPQR) working with local centers and Accreditation Canada to set quality standards. There is great potential for future international collaborations through such quality initiative programs or the work being done by the CARO Human Resources & Standards Committee to track supply and demand for oncology services.

While we have just returned home from Newfoundland and Labrador, the focus has already shifted to future goals and celebrating next year’s accomplishments at the 2015 CARO ASM in beautiful Kelowna BC.

Dr Ross Halperin
BC Cancer Agency
Kelowna, Canada

Dr Amanda Caissie
Dalhousie University
Saint John Newfoundland, Canada
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A digest of essential reading for all radiation oncologists

BY PHILIPPE LAMBIN, DIRK DE RUYSSCHER AND HANS KAANDERS
PURPOSE
Adjuvant therapy with an aromatase inhibitor improves outcomes, as compared with tamoxifen, in postmenopausal women with hormone-receptor-positive breast cancer.

METHODS AND MATERIALS
In two phase III trials, we randomly assigned premenopausal women with hormone-receptor-positive early breast cancer to the aromatase inhibitor exemestane plus ovarian suppression or tamoxifen plus ovarian suppression for a period of five years. Suppression of ovarian oestrogen production was achieved with the use of the gonadotropin-releasing-hormone agonist triptorelin, oophorectomy, or ovarian irradiation. The primary analysis combined data from 4,690 patients in the two trials.

RESULTS
After a median follow-up of 68 months, disease-free survival at five years was 91.1% in the exemestane-ovarian suppression group and 87.3% in the tamoxifen-ovarian suppression group (hazard ratio for disease recurrence, second invasive cancer, or death, 0.72; 95% confidence interval [CI], 0.60 to 0.85; P<0.001). The rate of freedom from breast cancer at five years was 92.8% in the exemestane-ovarian suppression group, as compared with 88.8% in the tamoxifen-ovarian suppression group (hazard ratio for recurrence, 0.66; 95% CI, 0.55 to 0.80; P<0.001). With 194 deaths (4.1% of the patients), overall survival did not differ significantly between the two groups (hazard ratio for death in the exemestane-ovarian suppression group, 1.14; 95% CI, 0.86 to 1.51; P=0.37). Selected adverse events of grade 3 or 4 were reported for 30.6% of the patients in the exemestane-ovarian suppression group and 29.4% of those in the tamoxifen-ovarian suppression group, with profiles similar to those for postmenopausal women.

CONCLUSIONS
In premenopausal women with hormone-receptor-positive early breast cancer, adjuvant treatment with exemestane plus ovarian suppression, as compared with tamoxifen plus ovarian suppression, significantly reduced recurrence.

FUNDING
National HealFunded by Pfizer and others; TEXT and SOFT ClinicalTrials.gov numbers, NCT00066703 and NCT00066690, respectively.
**BACKGROUND**
We investigated whether 18 months of androgen suppression plus radiotherapy, with or without 18 months of zoledronic acid, is more effective than 6 months of neoadjuvant androgen suppression plus radiotherapy with or without zoledronic acid.

**METHODS**
We did an open-label, randomized, \(2 \times 2\) factorial trial in men with locally advanced prostate cancer (either T2a N0 M0 prostatic adenocarcinomas with prostate-specific antigen [PSA] ≥10 μg/L and a Gleason score of ≥7, or T2b-4 N0 M0 tumours regardless of PSA and Gleason score). We randomly allocated patients by computer-generated minimisation-stratified by centre, baseline PSA, tumour stage, Gleason score, and use of a brachytherapy boost-to one of four groups in a 1:1:1:1 ratio. Patients in the control group were treated with neoadjuvant androgen suppression with leuprorelin (22.5 mg every 3 months, intramuscularly) for 6 months (short-term) and radiotherapy alone (designated STAS); this procedure was either followed by another 12 months of androgen suppression with leuprorelin (intermediate-term; ITAS) or accompanied by 18 months of zoledronic acid (4 mg every 3 months for 18 months, intravenously; STAS plus zoledronic acid) or by both (ITAS plus zoledronic acid). The primary endpoint was prostate cancer-specific mortality. This analysis represents the first, preplanned assessment of oncological endpoints, 5 years after treatment. Analysis was by intention-to-treat. This trial is registered with ClinicalTrials.gov, number NCT00193856.

**FINDINGS**
Between 20 Oct 2003 and 15 Aug 2007, 1,071 men were randomly assigned to STAS (n=268), STAS plus zoledronic acid (n=268), ITAS (n=268), and ITAS plus zoledronic acid (n=267). Median follow-up was 7.4 years (IQR 6.5-8.4). Cumulative incidences of prostate cancer-specific mortality were 4.1% (95% CI 2.2-7.0) in the STAS group, 7.8% (4.9-11.5) in the STAS plus zoledronic acid group, 7.4% (4.6-11.0) in the ITAS group, and 4.3% (2.3-7.3) in the ITAS plus zoledronic acid group. Cumulative incidence of all-cause mortality was 17.0% (13.0-22.1), 18.9% (14.6-24.2), 19.4% (15.0-24.7), and 13.9% (10.3-18.8), respectively. Neither prostate cancer-specific mortality nor all-cause mortality differed between control and experimental groups. Cumulative incidence of PSA progression was 34.2% (28.6-39.9) in the STAS group, 39.6% (33.6-45.5) in the STAS plus zoledronic acid group, 29.2% (23.8-34.8) in the ITAS group, and 26.0% (20.8-31.4) in the ITAS plus zoledronic acid group. Compared with STAS, no difference was noted in PSA progression with ITAS or STAS plus zoledronic acid; however, ITAS plus zoledronic acid reduced PSA progression (sub-hazard ratio [SHR] 0.71, 95% CI 0.53-0.95; p=0.021). Cumulative incidence of local progression was 4.1% (2.2-7.0) in the STAS group.
Long-term morbidity and quality-of-life scores were not affected adversely by 18 months of androgen suppression or zoledronic acid.

**INTERPRETATION**

Compared with STAS, ITAS plus zoledronic acid was more effective for treatment of prostate cancers with a Gleason score of 8-10, and ITAS alone was effective for tumours with a Gleason score of 7 or lower. Nevertheless, these findings are based on secondary endpoint data and post-hoc analyses and must be regarded cautiously. Long-term follow-up is necessary, as is external validation of the interaction between zoledronic acid and Gleason score. STAS plus zoledronic acid can be ruled out as a potential therapeutic option.

**FUNDING**

National Health and Medical Research Council of Australia, Novartis Pharmaceuticals Australia, Abbott Pharmaceuticals Australia, New Zealand Health Research Council, New Zealand Cancer Society, University of Newcastle (Australia), Calvary Health Care (Calvary Mater Newcastle Radiation Oncology Fund), Hunter Medical Research Institute, Maitland Cancer Appeal, Cancer Standards Institute New Zealand.
Purpose
Conflicting reports remain regarding the association between vasectomy, a common form of male contraception in the United States, and prostate cancer risk. We examined prospectively this association with extended follow-up and an emphasis on advanced and lethal disease.

Patients and Methods
Among 49,405 US men in the Health Professionals Follow-Up Study, age 40 to 75 years at baseline in 1986, 6,023 patients with prostate cancer were diagnosed during the follow-up to 2010, including 811 lethal cases. In total, 12,321 men (25%) had vasectomies. We used Cox proportional hazards models to estimate the relative risk (RR) and 95% CIs of total, advanced, high-grade, and lethal disease, with adjustment for a variety of possible confounders.

Results
Vasectomy was associated with a small increased risk of prostate cancer overall (RR, 1.10; 95% CI, 1.04 to 1.17). Risk was elevated for high-grade (Gleason score 8 to 10; RR, 1.22; 95% CI, 1.03 to 1.45) and lethal disease (death or distant metastasis; RR, 1.19; 95% CI, 1.00 to 1.43). Among a sub-cohort of men receiving regular prostate-specific antigen screening, the association with lethal cancer was stronger (RR, 1.56; 95% CI, 1.03 to 2.36). Vasectomy was not associated with the risk of low-grade or localised disease. Additional analyses suggested that the associations were not driven by differences in sex hormone levels, sexually transmitted infections, or cancer treatment.

Conclusion
Our data support the hypothesis that vasectomy is associated with a modest increased incidence of lethal prostate cancer. The results do not appear to be due to detection bias, and confounding by infections or cancer treatment is unlikely.
BACKGROUND
The European Randomised Study of Screening for Prostate Cancer (ERSPC) has shown significant reductions in prostate cancer mortality after nine years and 11 years of follow-up, but screening is controversial because of adverse events such as over-diagnosis. We provide updated results of mortality from prostate cancer with follow-up to 2010, with analyses truncated at 9, 11, and 13 years.

METHODS
ERSPC is a multicentre, randomised trial with a predefined centralised database, analysis plan, and core age group (55-69 years), which assesses prostate-specific antigen (PSA) testing in eight European countries. Eligible men aged 50-74 years were identified from population registries and randomly assigned by computer generated random numbers to screening or no intervention (control). Investigators were masked to group allocation. The primary outcome was prostate cancer mortality in the core age group. Analysis was by intention to treat. We did a secondary analysis that corrected for selection bias due to non-participation. Only incidence and no mortality data at nine years’ follow-up are reported for the French centres.

FINDINGS
With data truncated at 13 years of follow-up, 7,408 prostate cancer cases were diagnosed in the intervention group and 6,107 cases in the control group. The rate ratio of prostate cancer incidence between the intervention and control groups was 1.91 (95% CI 1.83-1.99) after nine years (1.64 [1.58-1.69] including France), 1.66 (1.60-1.73) after 11 years, and 1.57 (1.51-1.62) after 13 years. The rate ratio of prostate cancer mortality was 0.85 (0.70-1.03) after nine years, 0.78 (0.66-0.91) after 11 years, and 0.79 (0.69-0.91) at 13 years. The absolute risk reduction of death from prostate cancer at 13 years was 0.11 per 1,000 person-years or 1.28 per 1,000 men randomised, which is equivalent to one prostate cancer death averted per 781 (95% CI 490-1929) men invited for screening or one per 27 (17-66) additional prostate cancer detected. After adjustment for non-participation, the rate ratio of prostate cancer mortality in men screened was 0.73 (95% CI 0.61-0.88).

INTERPRETATION
In this update the ERSPC confirms a substantial reduction in prostate cancer mortality attributable to testing of PSA, with a substantially increased absolute effect at 13 years compared with findings after nine and 11 years. Despite our findings, further quantification of harms and their reduction are still considered a prerequisite for the introduction of population-based screening.


Lancet. 2014 Aug 07. [Epub ahead of print]
**PROSTATE**

Ipilimumab versus placebo after radiotherapy in patients with metastatic castration-resistant prostate cancer that had progressed after docetaxel chemotherapy (CA184-043): a multicentre, randomised, double-blind, phase III trial.


**BACKGROUND**
Ipilimumab is a fully human monoclonal antibody that binds cytotoxic T-lymphocyte antigen 4 to enhance antitumour immunity. Our aim was to assess the use of ipilimumab after radiotherapy in patients with metastatic castration-resistant prostate cancer that progressed after docetaxel chemotherapy.

**METHODS**
We did a multicentre, randomised, double-blind, phase III trial in which men with at least one bone metastasis from castration-resistant prostate cancer that had progressed after docetaxel treatment were randomly assigned in a 1:1 ratio to receive bone-directed radiotherapy (8 Gy in one fraction) followed by either ipilimumab 10 mg/kg or placebo every three weeks for up to four doses. Non-progressing patients could continue to receive ipilimumab at 10 mg/kg or placebo as maintenance therapy every three months until disease progression, unacceptable toxic effect, or death. Patients were randomly assigned to either treatment group via a minimisation algorithm, and stratified by Eastern Cooperative Oncology Group performance status, alkaline phosphatase concentration, haemoglobin concentration, and investigator site. Patients and investigators were masked to treatment allocation. The primary endpoint was overall survival, assessed in the intention-to-treat population. This trial is registered with ClinicalTrials.gov, number NCT00861614.

**FINDINGS**
From 26 May 2009 to 15 Feb 2012, 799 patients were randomly assigned (399 to ipilimumab and 400 to placebo), all of whom were included in the intention-to-treat analysis. Median overall survival was 11.2 months (95% CI 9.5-12.7) with ipilimumab and 10.0 months (8.3-11.0) with placebo (hazard ratio [HR] 0.85, 0.72-1.00; p=0.053). However, the assessment of the proportional hazards assumption showed that it was violated (p=0.0031). A piecewise hazard model showed that the HR changed over time: the HR for 0-5 months was 1.46 (95% CI 1.10-1.95), for 5-12 months was 0.65 (0.50-0.85), and beyond 12 months was 0.60 (0.43-0.86). The most common grade 3-4 adverse events were immune-related, occurring in 101 (26%) patients in the ipilimumab group and 11 (3%) of patients in the placebo group. The most frequent grade 3-4 adverse events included diarrhoea (64 [16%] of 393 patients in the ipilimumab group vs seven [2%] of 396 in the placebo group), fatigue (40 [11%] vs 35 [9%]), anaemia (40 [10%] vs 43 [11%]), and colitis (18 [5%] vs 0). Four (1%) deaths occurred because of toxic effects of the study drug, all in the ipilimumab group.

INTERPRETATION
Although there was no significant difference between the ipilimumab group and the placebo group in terms of overall survival in the primary analysis, there were signs of activity with the drug that warrant further investigation.

FUNDING
Bristol-Myers Squibb.
Randomized phase III trial of concurrent accelerated radiation plus cisplatin with or without cetuximab for stage III to IV head and neck carcinoma: RTOG 0522.


PURPOSE
Combining cisplatin or cetuximab with radiation improves overall survival (OS) of patients with stage III or IV head and neck carcinoma (HNC). Cetuximab plus platinum regimens also increase OS in metastatic HNC. The Radiation Therapy Oncology Group launched a phase III trial to test the hypothesis that adding cetuximab to the radiation-cisplatin platform improves progression-free survival (PFS).

PATIENTS AND METHODS
Eligible patients with stage III or IV HNC were randomly assigned to receive radiation and cisplatin without (arm A) or with (arm B) cetuximab. Acute and late reactions were scored using Common Terminology Criteria for Adverse Events (version 3). Outcomes were correlated with patient and tumour features and markers.

RESULTS
Of 891 analysed patients, 630 were alive at analysis (median follow-up, 3.8 years). Cetuximab plus cisplatin-radiation, versus cisplatin-radiation alone, resulted in more frequent interruptions in radiation therapy (26.9% versus 15.1%, respectively); similar cisplatin delivery (mean, 185.7 mg/m² versus 191.1 mg/m², respectively); and more grade 3 to 4 radiation mucositis (43.2% versus 33.3%, respectively), rash, fatigue, anorexia, and hypokalemia, but not more late toxicity. No differences were found between arms A and B in 30-day mortality (1.8% versus 2.0%, respectively; P = .81), 3-year PFS (61.2% versus 58.9%, respectively; P = .76), 3-year OS (72.9% versus 75.8%, respectively; P = .32), locoregional failure (19.9% versus 25.9%, respectively; P = .97), or distant metastasis (13.0% versus 9.7%, respectively; P = .08). Patients with p16-positive oropharyngeal carcinoma (OPC), compared with patients with p16-negative OPC, had better 3-year probability of PFS (72.8% versus 49.2%, respectively; P < .001) and OS (85.6% versus 60.1%, respectively; P < .001), but tumour epidermal growth factor receptor (EGFR) expression did not distinguish outcome.

CONCLUSION
Adding cetuximab to radiation-cisplatin did not improve outcome and hence should not be prescribed routinely. PFS and OS were higher in patients with p16-positive OPC, but outcomes did not differ.
BACKGROUND
We aimed to examine whether stereotactic radiosurgery without whole-brain radiotherapy (WBRT) as the initial treatment for patients with five to ten brain metastases is non-inferior to that for patients with two to four brain metastases in terms of overall survival.

METHODS
This prospective observational study enrolled patients with one to ten newly diagnosed brain metastases (largest tumour <10 mL in volume and <3 cm in longest diameter; total cumulative volume ≤15 mL) and a Karnofsky performance status score of 70 or higher from 23 facilities in Japan. Standard stereotactic radiosurgery procedures were used in all patients; tumour volumes smaller than 4 mL were irradiated with 22 Gy at the lesion periphery and those that were 4-10 mL with 20 Gy. The primary endpoint was overall survival, for which the non-inferiority margin for the comparison of outcomes in patients with two to four brain metastases with those with five to ten (HR 0.97, 95% CI 0.81-1.18 [less than non-inferiority margin], p=0.78; pnon-inferiority<0.0001). Stereotactic radiosurgery-induced adverse events occurred in 101 (8%) patients; nine (2%) patients with one tumour had one or more grade 3-4 event compared with 13 (2%) patients with two to four tumours and six (3%) patients with five to ten tumours. The proportion of patients who had one or more treatment-related adverse event of any grade did not differ significantly between the two groups of patients with multiple tumours (50 [9%] patients with two to four tumours vs 18 [9%] with five to ten; p=0.89). Four patients died, mainly of complications relating to stereotactic radiosurgery (two with one tumour and one each in the other two groups).
INTERPRETATION
Our results suggest that stereotactic radiosurgery without WBRT in patients with five to ten brain metastases is non-inferior to that in patients with two to four brain metastases. Considering the minimal invasiveness of stereotactic radiosurgery and the fewer side-effects than with WBRT, stereotactic radiosurgery might be a suitable alternative for patients with up to ten brain metastases.

FUNDING
Japan Brain Foundation.
Open versus laparoscopic surgery for mid-rectal or low-rectal cancer after neo-adjuvant chemoradiotherapy (COREAN trial): survival outcomes of an open-label, non-inferiority, randomised controlled trial.


BACKGROUND
Compared with open resection, laparoscopic resection of rectal cancers is associated with improved short-term outcomes, but high-level evidence showing similar long-term outcomes is scarce. We aimed to compare survival outcomes of laparoscopic surgery with open surgery for patients with mid-rectal or low-rectal cancer.

METHODS
The Comparison of Open versus laparoscopic surgery for mid or low REctal cancer After Neoadjuvant chemoradiotherapy (COREAN) trial was an open-label, non-inferiority, randomised controlled trial done between 4 April 2006 and 26 Aug 2009, at three centres in Korea. Patients (aged 18-80 years) with cT3N0-2M0 mid-rectal or low-rectal cancer who had received preoperative chemoradiotherapy were randomly assigned (1:1) to receive either open or laparoscopic surgery. Randomisation was stratified by sex and preoperative chemotherapy regimen. Investigators were masked to the randomisation sequence; patients and clinicians were not masked to the treatment assignments. The primary endpoint was three year disease-free survival, with a non-inferiority margin of 15%. Analysis was by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT0040951.

FINDINGS
We randomly assigned 340 patients to receive either open surgery (n=170) or laparoscopic surgery (n=170). Three year disease-free survival was 72.5% (95% CI 65.0-78.6) for the open surgery group and 79.2% (72.3-84.6) for the laparoscopic surgery group, with a difference that was lower than the prespecified non-inferiority margin (-6.7%, 95% CI -15.8 to 2.4; p<0.0001). 25 (15%) patients died in the open group and 20 (12%) died in the laparoscopic group. No deaths were treatment related.

INTERPRETATION
Our results show that laparoscopic resection for locally advanced rectal cancer after preoperative chemoradiotherapy provides similar outcomes for disease-free survival as open resection, thus justifying its use.

FUNDING
National Cancer Center, South Korea.
OESOPHAGEAL

Definitive chemoradiotherapy with FOLFOX versus fluorouracil and cisplatin in patients with oesophageal cancer (PRODIGE5/ACCORD17): final results of a randomised, phase II/III trial.


sensory neuropathy (24 [18%] vs one [1%], \( p < 0.0001 \)), increases in aspartate aminotransferase concentrations (14 [11%] vs two [2%], \( p = 0.002 \)), and increases in alanine aminotransferase concentrations (11 [8%] vs two [2%], \( p = 0.012 \)) were more common in the FOLFOX group, whereas serum creatinine increases (four [3%] vs 15 [12%], \( p = 0.007 \)), mucositis (35 [27%] vs 41 [32%], \( p = 0.011 \)), and alopecia (two [2%] vs 12 [9%], \( p = 0.005 \)) were more common in the fluorouracil and cisplatin group.

**INTERPRETATION**

Although chemoradiotherapy with FOLFOX did not increase progression-free survival compared with chemoradiotherapy with fluorouracil and cisplatin, FOLFOX might be a more convenient option for patients with localised oesophageal cancer unsuitable for surgery.

**FUNDING**

UNICANCER, French Health Ministry, Sanofi-Aventis, and National League Against Cancer.
ABSTRACT
There is increasing evidence supporting the role of genetic variants in the development of radiation-induced toxicity. However, previous candidate gene association studies failed to elucidate the common genetic variation underlying this phenotype, which could emerge years after the completion of treatment. We performed a genome-wide association study on a Spanish cohort of 741 individuals with prostate cancer treated with external beam radiotherapy (EBRT). The replication cohorts consisted of 633 cases from the UK and 368 cases from North America. One locus comprising TANC1 (lowest unadjusted P value for overall late toxicity = 6.85 × 10⁻⁹, odds ratio (OR) = 6.61, 95% confidence interval (CI) = 2.23-19.63) was replicated in the second stage (lowest unadjusted P value for overall late toxicity = 2.08 × 10⁻⁴, OR = 6.17, 95% CI = 2.25-16.95; P_{combined} = 4.16 × 10⁻¹⁰). The inclusion of the third cohort gave unadjusted P_{combined} = 4.64 × 10⁻¹¹. These results, together with the role of TANC1 in regenerating damaged muscle, suggest that the TANC1 locus influences the development of late radiation-induced damage.
BRACHYTHERAPY
Welcome to the Brachytherapy Corner.

In this edition of the newsletter you can read an article, authored by Max Peters from the University Medical Center Utrecht in The Netherlands, on focal brachytherapy for prostate cancer. The study analyzed the outcome of focal brachytherapy with iodine-125 sources after a local relapse. The possibilities of this emerging treatment modality are discussed.

In the September issue of the British Journal of Radiology a special edition on brachytherapy dosimetry was published. Antony Palmer, special feature editor, highlights the five articles that are presented. Read more to learn about the content. Finally, you will find the announcements for the second GEC-ESTRO workshop and the GEC-ESTRO in vivo dosimetry seminar that will take place in Brussels on 4–5 December 2014. Also you will find a final version of the workshop’s programme. Don’t forget to register for these interesting meetings.

We hope you will enjoy reading the Brachytherapy Corner.

Peter Hoskin, Bradley Pieters and Kari Tanderup
Focal salvage iodine-125 brachytherapy for prostate cancer recurrences after primary radiotherapy: A retrospective study regarding toxicity, biochemical outcome and quality of life

Max Peters
UMC Utrecht
Utrecht, The Netherlands
FOCAL SALVAGE IODINE-125 BRACHYTHERAPY FOR PROSTATE CANCER RECURRENTS AFTER PRIMARY RADIOTHERAPY: A RETROSPECTIVE STUDY REGARDING TOXICITY, BIOCHEMICAL OUTCOME AND QUALITY OF LIFE


Radiother Oncol., 2014;112:77-82.

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WHAT WAS YOUR MOTIVATION FOR INITIATING THIS STUDY?

The trend to focally ablate prostate cancer is increasing in the international literature, especially due to the advancements in the diagnostic area (e.g. PET, MRI, biopsies), which makes it possible to delineate tumours with increasing accuracy and excludes metastatic disease. Focal therapy, however, is predominantly directed at primary tumours.

The conducted analysis focuses on recurrences after a primary course of radiation treatment. In this setting (the so-called salvage setting), side-effects can be especially detrimental to the patient, since primary radiotherapy (external or internal) has already caused sometimes significant damage to the surrounding organs at risk (rectum, urethra, bladder, neurovascular bundles). A second whole-gland brachytherapy course is associated with significant toxicity rates of the gastrointestinal and genitourinary tract and erectile dysfunction. For this reason, whole-gland salvage is not commonly performed, and patients are treated with androgen deprivation therapy, a palliative strategy, which also carries the risk of major side-effects.

In theory, the focal approach could also be adopted for recurrent prostate cancer after primary radiotherapy (i.e. focal salvage), thereby decreasing toxicity patterns, while conserving cancer control. Preliminary small studies regarding focal salvage with different modalities have shown favourable trends in toxicity patterns so far.

WHAT WERE THE MAIN CHALLENGES DURING THE WORK?

Due to the retrospective nature of this analysis, data regarding prostate specific antigen (PSA) measurements, toxicity and quality of life were sometimes incomplete in our electronic information system. Various requests to obtain this data from urologists in different hospitals/clinics, primary care physicians, etc. had to be done to gather the most complete set of records available. Furthermore, a new planning and implantation system had been incorporated recently, which provided some difficulties in obtaining the dosimetry of the complete group from the old system.
WHAT ARE THE MOST IMPORTANT FINDINGS OF YOUR STUDY?
In line with the very small body of literature so far regarding focal salvage therapy, with varying techniques, the results of our study showed that only patient (5%) experienced a grade 3 urethral stricture in the late follow-up period (>90 days). This is very favourable compared to the grade 3 genitourinary toxicity patterns in whole-gland salvage series (up to 30%). Also, gastrointestinal toxicity was negligible and erectile dysfunction was not observed in the (only) five previously potent patients. Furthermore, biochemical failure rates were in line with whole-gland salvage and the focal salvage literature. Quality of life did not seem to decrease substantially compared to the situation before focal salvage. However, due to the highly technical procedure, with extensive pre-planning (functional MRI scans, necessary correlation with biopsies), only 20 patients have been treated so far in the last few years. Statistically, no clear recommendations can as of yet be made with regard to the right selection of patient eligible for focal salvage, as well as definitive treatment results compared to other types of salvage (whole-gland I-125 brachytherapy and other techniques).

WHAT ARE THE IMPLICATIONS OF THIS RESEARCH?
It is important to focus future research on answering the question which patients are most likely to benefit from a focal salvage approach compared to a whole-gland approach or androgen deprivation therapy. More data are needed in the diagnostic (predictive values of imaging techniques, biopsies, biochemical parameters/kinetics) and therapeutic domain (randomised trials between salvage approaches and modalities) to definitively answer the question whether we can offer a less toxic curative procedure for recurrent prostate cancer patients.
I have great pleasure in highlighting a collection of brachytherapy dosimetry review papers recently published in the September issue of the journal, BJR.

As we are all aware, there have been great developments in brachytherapy over the last decade and exciting prospects for future research, innovation and clinical implementation. The BJR special feature provides a timely review of current state-of-the-art research and prospects for future developments in a number of key areas of brachytherapy physics. The first article by Thorsten Sander [1] provides a unique and detailed overview of developments in reference dosimetry and dosimetric parameters for brachytherapy. Panagiotis Papagiannis et al [2], then provide a comprehensive discussion of state-of-the-art algorithms for brachytherapy treatment planning, explaining their concepts and limitations. Next, Chris Lee [3] reviews progress in best-practice brachytherapy treatment planning, in particular considering the incorporation of advanced imaging. Gustavo Kertzscher et al [4] then tackle the challenging prospect of in vivo verification of brachytherapy treatment delivery, reviewing trends, error detection capabilities, and prospects for the future. Finally, I have contributed a review of dosimetric audits in brachytherapy for safety and optimisation [5], considering previous audits, those currently in progress and future directions for independent physics review. Please take a look at my editorial in this issue for further details.

In putting this special feature together, I have had the great pleasure of working with expert authors alongside generous skilled reviewers. I hope you enjoy this collection of comprehensive articles on brachytherapy dosimetry.

Antony Palmer,
BJR Special Feature Editor

REFERENCES
1. Air kerma and absorbed dose standards for reference dosimetry in brachytherapy. T Sander
   The British Journal of Radiology 87 (1041), 20140176 doi: 10.1259/bjr.20140176
2. Current state of the art brachytherapy treatment planning dosimetry algorithms. P Papagiannis, E Pantelis, P Karaiskos
   The British Journal of Radiology 87 (1041), 20140163 doi: 10.1259/bjr.20140163
3. Recent developments and best practice in brachytherapy treatment planning. C D Lee
   The British Journal of Radiology 87 (1041), 20140146
doi: 10.1259/bjr.20140146
The British Journal of Radiology 87 (1041), 20140206
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September issue:
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Editorial:
2ND GEC-ESTRO WORKSHOP
4 December 2014, Brussels

Building on the success of the first workshop, ESTRO has decided to arrange a second one on 4 December 2014 also in Brussels. This one-day workshop will have a common theme where each of the GEC-ESTRO Working Groups (anorectal, brachyqs, breast, gynae, head & neck and prostate) will address the question: “State of art of brachytherapy to maximize the therapeutic window”. In addition all working groups will present their current most important work as posters.

Come and learn about our ongoing projects and take the opportunity of networking with like-minded brachytherapy enthusiasts.

Registration is free but the number of participants is limited.

www.estro.org/congresses-meetings/items/2nd-gec-estro-workshop>

GEC-ESTRO IN VIVO DOSIMETRY SEMINAR
5 December 2014, ESTRO office, Brussels

The seminar will focus on:
- Detectors for in vivo dosimetry
- Error detection methodologies
- Clinical implementation.

More information and how to participate: www.estro.org/congresses-meetings/items/gec-estro-in-vivo-dosimetry-seminar>
## Programme

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speakers</th>
</tr>
</thead>
<tbody>
<tr>
<td>08.30-08.45</td>
<td>Introduction: Jacob C. Lindegaard (DK), Chair GEC-ESTRO Committee</td>
<td>Peter Hoskin (UK), Past-Chair GEC-ESTRO Committee</td>
</tr>
<tr>
<td>08.45-10.00</td>
<td>BrachyQS - Moderator: Taran P. Paulsen (NO)</td>
<td>Impact of improvements in dosimetry on the therapeutic window. Frank-André Siebert (DE)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Approaches for reduction of uncertainties in brachytherapy to increase treatment quality. Marisol De Brabandere (BE)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Further potentials for high quality brachytherapy in the future. Frank Verhaegen (NL)</td>
</tr>
<tr>
<td>10.00-10.50</td>
<td>Anorectal - Moderator: Erik Van Limbergen (BE)</td>
<td>The role of brachytherapy in organ preservation for rectal cancer. Jean Pierre Gerard (FR)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dose response relationship in control of rectal cancer. Arthur Sun Myint (UK)</td>
</tr>
<tr>
<td>10.50-11.15</td>
<td>Coffee/tea</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Individualised prediction of morbidity: example of rectum nomogramme. Noha Jastaniya (AT)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Introducing the GEC ESTRO target volume concept in brachytherapy for vaginal cancer and vaginal recurrences. Remi Nout (NL)</td>
</tr>
<tr>
<td>12.30-14.00</td>
<td>Lunch</td>
<td></td>
</tr>
<tr>
<td>14.00-14.50</td>
<td>Head &amp; Neck - Moderator: Vratislav Strnad (DE)</td>
<td>ENT-COBRA: Update on the project. L. Tagliaferri (IT)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Interdisciplinary cooperation resulting in visual acuity preservation in ENT cancers. György Kovács (DE)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Breast brachytherapy: Target definition after closed cavity surgery - analysis of interobserver variability. K. Lössl (CH)</td>
</tr>
<tr>
<td>15.40-16.05</td>
<td>Coffee/tea</td>
<td></td>
</tr>
<tr>
<td>16.05-17.20</td>
<td>Urogec - Moderator: Bradley Pieters (NL)</td>
<td>Five year Laparoscopic and Robot-Assisted bladder implants - The alternative. Elzbieta van der Steen (NL) &amp; Geert Smits (NL)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prostate brachytherapy: the evolution from whole gland boost to focal salvage. Roberto Alonzi (UK)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prostate brachytherapy: the evolution from whole gland boost to focal salvage. Peter Hoskin (UK)</td>
</tr>
<tr>
<td>17.20</td>
<td>Closing Remarks: Christian Kirisits (AT), Chair-elect GEC-ESTRO Committee</td>
<td></td>
</tr>
</tbody>
</table>

GEC-ESTRO would like to thank our sponsors, Eckert & Ziegler BEBIG, Elekta Brachytherapy and Varian Medical Systems for their support in the organisation of this workshop and in the activities of this Committee.
PHYSICS
Welcome to the Physics Corner

We are pleased to have four very diverse and interesting topics in this edition. Alina Santiago introduces a freely available app, developed by the Aarhus Particle Therapy Group to look up ion stopping powers and to calculate ranges. In an interview with Anne Vestergaard, the importance of the role of a medical physicist in the clinical implementation of adaptive radiotherapy is demonstrated nicely. On the research side, two recently published papers are highlighted in the editors’ picks session. And last but not least, we recommend physicists and related professionals who are pursuing a career in research and development to read the introduction to the ESTRO research master class by Ben Heijmen.

Ludvig Muren (ludvmure@rm.dk),
Frank Van den Heuvel (frank.vandenheuvel@oncology.ox.ac.uk),
Misch Hoogeman (m.hoogeman@erasusmc.nl)

**PHYSICS MEMBERS ASSEMBLY**
Saturday 25 April 2015 at the 3rd ESTRO Forum, Barcelona
13.30-14.30
Imagine you are in the gantry room of your new proton therapy facility, and you want to measure the lateral penumbra of your 230 MeV proton beam. While setting up the polymethyl-methacrylate (PMMA) blocks, you try to recall at which position you should place the EBT (External Beam Therapy) film. Or imagine you have been granted beamtime at a carbon ion facility. During a preparatory meeting you discuss what ion energy range you need in order to have a spread out Bragg peak from 10-15 cm in your water phantom. And, just what is the linear energy transfer (LET) of a 421.8 MeV/u carbon ion beam? Worry no more: a new app “Electronic stopping power” for Android devices looks up stopping powers using the International Commission on Radiation Units and Measurements (ICRU) 49 (protons and alphas) and the revised ICRU 73 (lithium and heavier ions). In addition, MSTAR (program for calculation of electronic stopping powers for heavy ions) and an implementation of the Bethe equation expanded to low energies are also available. The latter must be used with care since this algorithm, although valid for every projectile/target combination, leads in specific cases to large deviations from existing experimental data.

The app knows all ICRU materials, and expands the ICRU and MSTAR data using Bragg’s additivity rule when possible. Ranges are calculated using the continuous slowing down approximation (CSDA), and a nifty feature is included enabling inverse look-ups, i.e. you can determine what projectile energy is needed for a given range. Additionally the calculated range is in g/cm², independent of target density; an estimation of the range in cm for materials other than water would be recommendable for future versions.

The app is available on Google Play for free, and only requires USB storage access for saving the stopping power tables; however, it can lead to a crash if it is installed on a mobile without external storage. This will, I hope, be fixed with a future update to the app. No network connection is needed, making the app usable even when in WiFi-free zones.

The app is based on the stopping power library libdEdx, which is hosted on sourceforge.net. Both the app and the libdEdx library are open source and were developed by the Aarhus Particle Therapy Group.

The app is available with this link: https://play.google.com/store/apps/details?id=dk.au.aptg.dEdx

Alina Santiago
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Anne Vestergaard started her career in medical physics in 1998 and has been working at Aarhus University Hospital (AUH) in Denmark since 2001. In this interview we learn about how Anne and her colleagues at AUH implemented image guided and adaptive radiotherapy.

**What is the most obvious reason for delivering adaptive radiotherapy?**
When treating patients with daily online cone beam computed tomography (CBCT), we discovered large variations in the patient anatomy compared to the pre-treatment planning CT. Several studies have shown this variability in the patient anatomy, but when the effect is revealed on the treatment fraction level, and you have the ability to change the treatment accordingly it seems obvious to do so. In the beginning this was performed in an unsystematic way and only systematically for head and neck cancer, where a mid-course CT was introduced in 2006 in order to decide whether or not to adapt the treatment.

**Can you mention some examples?**
We have seen head and neck cancer patients with large tumour shrinkage receiving an increased dose to the spinal cord [1]. When preparing for hands-on training of the radiation therapists (RTT’s), we found bladder cancer patients with several fractions, where not even our very large population-based margins were sufficient. For lung cancer patients we have seen changes such as atelectasis and pneumonia, which can change the target position and/or the dose distribution considerably.

**How did you get involved with the implementation of adaptive radiotherapy?**
I became involved with the implementation of image guided radiotherapy (IGRT) using kV-kV images for daily setup in 2008, where patients with cancers in the head and neck, brain, thorax and pelvic regions went from portal image verification at first fraction as standard to daily online IGRT. We developed a program for the training of RTTs, which we have further developed for CBCT guided IGRT as well as adaptive radiotherapy [2]. In 2009 CBCT-based IGRT was implemented for the same very large patient group [3].

**What was your first project on adaptive radiotherapy for bladder cancer?**
In 2010, Dr Jimmi Søndergaard MD, PhD, conducted a clinical trial with tumour boost guided by Lipiodol injected into the bladder wall [4]. Jimmi and I performed a retrospective study comparing different strategies for adaptive radiotherapy using plan selection for the treatment of urinary bladder cancer [5]. After the study period I thought that it would be very interesting to see the adaptive strategy implemented in the clinic for the benefit of the patients. In 2012 a ▼
Who is involved in the trial and how does it recruit?
Three Danish centres are recruiting: Odense University hospital, Copenhagen University Hospital, Herlev and Aarhus University Hospital. We have now included 62 patients and are aiming for 65 patients. The trial is expected to close by the end of this year. In June this year the results from the first 20 patients were published [6].

What are the future plans for trials or research?
We are planning a multicentre clinical trial combining adaptive radiotherapy with the Lipiodol-guided boost to the tumour. Ongoing studies are performed to reveal the effect of intra-fractional motion in online plan selection. At ESTRO 33 in Vienna we presented a study showing that, although large intra-fractional changes were present for the first ten patients in the protocol, the fact that the selected plan always encompassed the bladder with more than the 5 mm applied margin resulted in coverage in 97% of the cases and the few cases where the bladder wasn’t covered were where the patient had a very large bladder extending outside the largest planning target volume (PTV) at the first scan.

Are there other sites you are treating with adaptive radiotherapy?
Yes, in April 2013 we implemented adaptive radiotherapy (ART) for lung cancer using daily soft tissue match on the tumour and we decreased the margin for treating the tumour site. The position of the involved lymph node(s) is evaluated using a match structure [7, 8]. Patients are re-planned if large anatomical changes are detected or if the relative position between the tumour and the lymph node deviates outside a given limit.

Do you have any future plans for ART in other treatment sites?
We have groups working on locally advanced prostate cancer [9], cervical cancer and rectal cancer, but none of them are currently ready for clinical implementation.

REFERENCES
Toward adaptive radiotherapy for head and neck patients: feasibility study on using CT-to-CBCT deformable registration for “dose of the day” calculations

Catarina Veiga

Dosimetric consequences of intrafraction prostate motion in scanned ion beam radiotherapy

Filippo Ammazzalorso
TOWARD ADAPTIVE RADIOTHERAPY FOR HEAD AND NECK PATIENTS: FEASIBILITY STUDY ON USING CT-TO-CBCT DEFORMABLE REGISTRATION FOR “DOSE OF THE DAY” CALCULATIONS


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What was your motivation for initiating this study?
Dealing with deformation is one of the main challenges in treating head and neck (HN) malignancies. The day-to-day changes in anatomy can compromise the objectives of the particular treatment, and it is recognised that for some patients the treatment needs to be replanned. Replanning brings additional clinical workload and requires the acquisition of a new computed tomography (CT) scan, so it is important to understand which patients will benefit the most from adaptation and when to intervene. Ideally the need for adaptation should be routinely evaluated based on the dose that has already been delivered “dose of the day”. Therefore, we investigated the use of CT-to-cone-beam CT (CBCT) deformable image registration (DIR) to estimate the “dose of the day” received by a HN patient.

What are the implications of this research?
This work presents a first step towards an online and automated adaptive radiotherapy workflow based on DIR and CBCT imaging. The results obtained add confidence in translating the use of non-rigid registration to clinical routine. A long term goal is to remove the need to acquire a new CT scan for replanning.

What is the most important finding of your study?
The findings from our study showed that using DIR to deform the planning CT scan to match a daily CBCT image resulted in similar dose calculations to those performed on a new CT. The dose differences were within clinically acceptably values, and the method outperformed using rigid-only registration and calibrated CBCT images.

What were the challenges during the work?
Validating DIR for clinical applications is very challenging due to the lack of gold standards. Therefore, we performed two independent tests to assess the suitability of CT-to-CBCT registrations for the application proposed. First, a geometric evaluation based on expert knowledge to assess the ability to align features between CT and CBCT images. Secondly, a dosimetric comparison to show that the deformed CT was equivalent to a rescan CT as far as dose calculation is concerned.
What was your motivation for initiating this study?
Our group is carrying out a series of dosimetric investigations, supervised by Dr Urszula Jelen, all aiming at the accurate and safe treatment at the upcoming proton and carbon ion therapy centre of Marburg. The prostate is among our future planned indications for scanned ions, but its irregular and unpredictable motion represents a challenge, because of interplay effects. These have been extensively researched for targets affected by regular respiratory motion, but there was a knowledge gap for the prostate, which our study has tried to address.

What where the challenges during the work?
As part of our effort to deliver a clinically realistic assessment, we used data from implanted radiofrequency beacons, courtesy of Professor Katja Langen of the University of Maryland School of Medicine. Currently this is the only way of recording prostate motion over an entire treatment course, with high temporal and spatial resolution, but whose signal is not directly usable by the treatment planning system. So we had to develop an ad hoc 4D dose computation approach, to combine the motion data and beam scanning information, while correctly accounting for the complex relative biological effectiveness of carbon ions.

What is the most important finding of your study?
For us, at the present time, the most clinically valuable result is knowing that, even with interplay effects caused by significant prostate motion, appropriate safety margins and a reasonable fractionation regime are likely to yield adequate target coverage. In addition, we have investigated the validity of various countermeasures, both at planning and delivery time, and this information can help us and the community define future carbon ion clinical protocols for prostate cancer treatment.

What are the implications of this research?
For the first time we have realistic dosimetric information on prostate treatment with a scanned ion beam, under a variety of planning and delivery scenarios, that anybody can use to prioritise future research directions, both clinical and technical. From our perspective, since the tools we developed for the study are also suitable for retrospective dose verification on a daily basis, we are considering investigating their application to offline adaptive strategies. In the light of our results, this is a promising option, at least until on-line motion compensation becomes a clinical reality.
NEW ESTRO TEACHING COURSE IN 2015

RESEARCH MASTERCLASS IN RADIOThERAPY PHYSICS

3 - 6 September 2015
Prague, Czech Republic

Interview with Ben Heijmen,
Course director

Why was this course created?
The majority of ESTRO courses for physicists have a focus on the competencies, skills and knowledge required for clinical practice. On the other hand, physics research and development (R&D) has greatly contributed to the development of radiotherapy in the past decades, and ESTRO wants to promote research activities among young physicist members. The ESTRO Research Masterclass in Radiotherapy Physics was therefore created for this purpose.

What are the main learning outcomes?
Attendees of the Masterclass will submit a proposal or idea for a research project or a scientific paper to be discussed and further improved upon, under the supervision of a team of internationally renowned scientists/teachers. By discussing real scientific proposals and ideas attendees will learn from their peers and the attending faculty, how to turn an initial idea into a successful project with scientific output. In addition, for a broad range of radiotherapy research fields, expert faculty members will highlight current trends and discuss...
important unresolved issues with future research opportunities. Some general aspects of scientific research (for example, writing scientific papers and grant applications) will also be covered by lectures. Ample time will be allowed for discussions with fellow attendees and faculty members (including in the evenings), allowing the development of new, potentially long lasting, scientific/mentorship relationships.

**How did you select the teachers?**
First of all, I want to state that I am extremely proud of the selected faculty. Without exemption, they are all great scientists and leaders in their field. Moreover, they are all excellent teachers and highly experienced in guiding students and young investigators. The selection of the faculty members was based on the following criteria:
1. Excellent R&D track record and teaching skills
2. Preference for (hands-on) specialists rather than generalists
3. Good spread between topics in the field
4. Gender balance
5. Not too close to the end of their career
6. Sufficient balance regarding nationalities and institutions.

**Who should attend?**
This Research Masterclass aims at supporting individuals beginning research and setting up a career in radiotherapy physics or a related field (imaging science, computer science, mathematics, or biophysics). The target group should have up to approximately seven years of experience and pursue a full-time research position, or a combination of research with a (future) clinical position, e.g. as a medical physicist.
A warm welcome to this issue of the RTT Corner.

In the last issue of the RTT Corner we published the first part of an interview with the ESTRO President, Professor Philip Poortmans. I hope you all had enough patience to wait for the second part of this interview which you can read in the following pages. It will be worth waiting for, I can assure you.

The second article is a review by Danilo Pasini of recently published scientific papers that are of interest for the radiation therapists (RTT) community: one paper is on auto contouring and the second article focuses on lateral patient positioning in the breast. So, whatever your role is as an RTT within the clinic, these articles are not to be missed.

The final article is a report on a project that was run for RTTs to improve their skills and knowledge about research. This very successful project was carried out at the Aarhus University Hospital in Denmark. In this article Annette Boejen clearly describes the goals and results of this project. I would like to thank Danilo Pasini and Annette Boejen for their kind contributions to this issue of the newsletter.

Finally I’m very happy to welcome on board Philipp Scherer who will as of now join me as co-editor of the RTT Corner. Get to know Philipp on the next page where he tells us a bit about himself and his background. Together we’ll work to prepare for you every two months a most up-to-date RTT Corner. And by the way, if you also want to share your experiences and thoughts, don’t hesitate to send us an email (m.kamphuis@amc.nl and p.scherer@salk.at).

Martijn Kamphuis
I would like to take this opportunity to introduce myself as a new member of the ESTRO newsletter team. There was an introductory article about me recently published in this newsletter when I joined the RTT Committee, so I’ll try to keep this short.

I am the ESTRO liaison representative for the radiation therapists (RTTs) based in Austria. Recently, I have been able to extend my role within the ESTRO family by taking up the position of observer on the RTT committee. At the moment, my foremost aims as an observer are to get a deeper insight into the work of the committee and to support its members. Therefore, I’m glad that I have the opportunity to support Martijn as co-editor of the ESTRO newsletter in the future.

I graduated in 2005 and completed my MSc in radiotherapy and oncology at the Sheffield Hallam University in the UK this year. I am currently working in the Department of Radiotherapy and Radio-Oncology at the Paracelsus Medical University Clinics at the Salzburg Landeskliniken, where I started as an RTT on the treatment floor immediately after my graduation. Since then, my job description has extended and I am glad to work with, support and lead a team of 20 RTTs on the treatment floor now (still in the same department). As well as my involvement in ESTRO, I am the current Chair of the ÖGRO ARGE RT, the national platform for RTTs in Austria. My main areas of interest and expertise include image-guided radiation therapy (IGRT) and immobilisation as well as patient care in general and continuous professional development (CPD).

Philipp Scherer
Landeskliniken
Salzburg, Austria
How do you look upon the role of the RTT within the interdisciplinary team?

Within the multidisciplinary team the radiation oncologist represents the department. At an interdisciplinary level, the clinical radiotherapy treatment is performed by a team consisting of doctors, physicists and RTTs. A clear shift of activities and responsibilities has taken place. I used to do simulation, make contours and masks, and finally plan and treat the patient by myself. Nowadays, only the medical part is taken care of by the doctor. Treatment preparation is now a split responsibility between physicists and RTTs. Normally, I contour the breast on CT by myself, but I also let RTTs perform this activity. I completely trust them; they really know how to work according to the prevailing protocols.

So, if a task is well described and protocolled, would you say that many tasks can be delegated to the RTT group?

Yes, absolutely. It must be said that the legal responsibility was and will continue to be in the hands of the radiation oncologist. But in the execution of radiotherapy many tasks can be delegated, and not only the boring and repetitive ones. It’s just a matter of dividing the tasks.

Previously, most delineation activities were performed by the doctor. More recently, the delineation of organs at risk (OAR) is now done by RTTs. The next step will be that the auto-contouring programmes will take over the largest part of target delineation. Probably in the first place this will be supervised by a doctor. Later on a two-step procedure is likely. First the created contours will be thoroughly examined by an RTT. Secondly a doctor will make a final safety check. Delegating the delineation of treatment targets to RTTs is difficult. But I can imagine that clinical target volume (CTV) definition in breast, provided a well...
described guideline is available, could be perfectly performed by RTTs. Trained RTTs are very well capable of working according to guidelines, independent of the structure they concern. Good guidelines are key. First in order to be sure that the proper parts are delineated, and second, to reduce the inter-observer variation not just between colleagues, but also between institutes and disciplines.

The shift of tasks is not only visible in treatment preparation but also in treatment planning. This aspect of radiotherapy is more and more performed by so-called dosimetrist. Personally I believe that the Dutch way, in which specialised RTTs take care of this part of the radiotherapy treatment, really works. I’m really pleased with the quality of the treatment plans that are made. I look upon RTTs working in other parts of the treatment like CT simulation or on the linear accelerator in the same manner. Usually planning RTTs were considered to be the best of the RTTs. Nowadays this has completely changed. For me the RTT taking care of innovation is taking this position. But this is, as in other disciplines, a minority of the group.

Putting it all together, the RTT plays a key role in radiotherapy treatment. Assessment and analyses of in room imaging for insistance can be well performed by RTTs. Standardisation makes task delegation possible.

Where should RTTs most effectively focus their activities on?
First of all I have to think about the process of implementing lean management. When this started in my department I was very critical. But in the end it really worked. Processes became easy and more efficient. Patients are now able to go through the therapy chain not only in a faster but also a safer manner. Due to that development, more time is available for other activities.

Secondly, I’m thinking of improving the knowledge on side-effects and outcomes. In many countries it is now mandatory to record outcome and complications. In my institute RTTs take part in the discussions of these subjects. Through this, they improve their knowledge on how patients are doing after the treatment. This is very useful, since RTTs don’t usually meet patients in their follow-up phase.

If the knowledge and involvement of RTTs have improved, as a consequence, are they according to you able to give feedback to the doctor?
Absolutely, and more importantly, to the patient. Who sees the patient the most frequently during treatment? It’s the RTT who delivers the treatment. If for instance, no skin reaction takes place in hypo fractionated treatment for the breast, it is still very possible for it to occur four to five weeks after treatment. This is something that RTTs should know. With this knowledge, better care can be delivered, especially since the RTT has a key role within the information provision process.

How do you see the involvement of RTTs in the field of research?
These are the things I really like to see. RTTs are taking care of innovative projects, like optimising and creating new planning techniques. And also other projects are possible, sometimes starting via a Bachelor thesis. These projects can be the trigger to make a change in the treatment process, for instance in logistics.
Paper review by Danilo Pasini
Poli. Univ. Gemelli
Rome, Italy

Recommendation for a contouring method and atlas of organ at risk in nasopharyngeal carcinoma patients receiving intensity-modulated radiotherapy


Whole breast radiotherapy in the lateral decubitus position: a dosimetric and clinical solution to decrease the doses to the organs at risk (OAR)

RECOMMENDATION FOR A CONTOURING METHOD AND ATLAS OF ORGAN AT RISK IN NASOPHARYNGEAL CARCINOMA PATIENTS RECEIVING INTENSITY-MODULATED RADIOTHERAPY


BACKGROUND

Contouring organs at risk (OAR) in the head and neck (H&N) cancer patient has always been difficult and complex in terms of variability and the different interpretation of the delineation. In the era of auto-contouring systems based on the use of atlases, which appear to decrease the operator variability, it is fundamental to reach a consensus on how the different structures must be delineated and what contours must be included. This is especially important in the head and neck region in order to facilitate a series of uniform and comparable dosimetric parameters to correlate with the side effects induced by radiotherapy.

In this study, two to four delineation methods on 41 nasopharyngeal carcinoma (NPC) patients were compared using atlas-based auto-contouring (ABAS) auto-contouring system (Elekta CMS) and then corrected and reviewed by two experts. They based their evaluation not only on the anatomical boundaries but also on the radiation induced injury.

METHODS

A literature review was performed for OAR in H&N delineations identifying two to four contouring methods for temporal lobe, parotid gland, spinal cord, inner and middle ear. Each contouring method included different anatomical parts of the structure in the delineation. The authors applied the different methods to 41 non-metastatic NPC patients using ABAS, following by expert review. They contoured gross target volume (GTV) and clinical target volume (CTV) according to International Commission on Radiation Units and Measurements (ICRU) guidelines and also contoured the OARs. To each delineation (CTV and OARs), they added a 3mm margin to generate the corresponding planning target volume and planning organs at risk volume (PTV/PRV), respectively. Statistical analyses were used to compare all the dosimetric parameters.

FINDINGS

Significant differences in both the absolute volume and selected parameters of all organs were observed using the different contouring methods. This means that different contouring methods heavily influence planning optimisation and the correlation between dose and side effects. This is particularly evident in this study because the OARs are in close proximity to the CTV and they take into account not only the inter-observer variability but also the subjective diversity of OAR.
interpretation. The inclusion of the structure to be contoured according to the probability of radiotherapy-induced injuries in the different organs is also interesting. The authors summarised their findings by providing a clear table of the anatomical boundaries of the structures, including the sub-structures, which must be included or not according to the possibility of side-effects at follow up.

RELEVANCE TO RADIATION THERAPISTS (RTTS)
Identification of OARs, especially in intensity modulated radiotherapy (IMRT) treatment, is needed for precise planning optimisation. Dosemetrists and RTTs involved in contouring activity must have an advanced knowledge of the most recent development of guidelines on this topic. Despite the use of auto-contouring systems, the definition of atlases based on consensus guidelines and the review and correction of the delineations remain of importance and have to be managed by the RTTs.
WHOLE BREAST RADIOTHERAPY IN THE LATERAL DECUBITUS POSITION: A DOSIMETRIC AND CLINICAL SOLUTION TO DECREASE THE DOSES TO THE ORGANS AT RISK (OAR)


BACKGROUND
The set-up of breast cancer patients is one of the most commonly investigated radiotherapy treatments. Different techniques and patient positions, with the aim of reaching better organ at risk (OAR) sparing, less toxicity and acceptable reproducibility, are regularly investigated. In this study, the feasibility of the lateral decubitus position was investigated.

METHODS
The authors adopted the lateral decubitus position for patients with large and pendulous breasts, using a positioning system purpose built for this technique (LD Board by Techset).

Fifty-six patients were placed in the lateral decubitus position on this dedicated board with a back rest, a carbon angled support to place under the breast to be treated and a large elastic fabric band used to flatten and move the contralateral breast. Radio-opaque markers were used to mark the medial border and the apex of the breast. They acquired a CT-scan in this position and created a 3D treatment plan using 4 or 6 MV energy beams and 15/20 dynamic wedge to have a homogeneous dose distribution.

The breast position was checked weekly by portal images and the accuracy was evaluated by measuring the distance between the field borders and anatomical markers.

FINDINGS
The most relevant result was that breast treatment was feasible in the lateral decubitus position, although the accuracy and reproducibility of the technique was not reported upon in the article.

From a dosimetric point of view, the investigators achieved an acceptable dose homogeneity due to better conformation of the breast as it lays to the side of the patient and assumed a flat shape. The dose to the considered OARs (ipsilateral lung and heart) was very low, as expected. Moreover they noticed a good result in terms of toxicity and clinical outcome. They achieved an acceptable dose distribution by means of 3D CRT (conformal radiation therapy), often without segmental fields (field in field) or without intensity modulated radiotherapy (IMRT) techniques that both increase the skin dose and the incidence of dermatitis.
RELEVANCE TO RADIATION THERAPISTS (RTTS)

Patient setup is universally recognised as being the responsibility of the RTT. In this paper there are some insights that could lead to further investigation of the setup reproducibility and data collection on the accuracy of treatment. The paper underlines the necessity for RTTs and the radiotherapy team to manage different techniques, patient setups and positioning systems for the same tumour site (anatomical site), in order to choose the right solution for each patient based on their individual needs.
RESEARCH METHODOLOGY FOR RADIATION THERAPISTS

A course report on quantitative research methods - based on project-oriented learning

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“Reading articles I am thinking quite differently and critically - and by discussions on evaluation of clinical topics, I am immediately a step or two ahead.” (Feedback from one of the participants)

INTRODUCTION

The implementation of new high-tech treatments with contouring of organs at risk, dose planning, independent decisions about treatment performance from image-guided radiation therapy and related interventions are new areas where radiation therapists (RTTs) have been given an increased responsibility in recent years. In addition to their technical tasks, RTTs have contact, observe and communicate with patients every day.

As members of a multi-disciplinary team, RTTs can contribute to research, ensuring that patients receive the best treatment based on the most comprehensive knowledge.

In 2008-2009, an interdisciplinary group of scientists and heads of education and clinical practice at department of Oncology, Aarhus University Hospital started discussions about involving experienced RTTs in research activities. How could this be developed and implemented in clinical practice? The result ended up as a project: “Research Methodology for Radiation Therapists – a course in quantitative research methodology based on problem-oriented learning”. The course was evaluated to be equivalent to 15 ECTS points.

PURPOSE AND AIM

The purpose of the course was to introduce the participants to scientific problem-oriented thinking in quantitative research methodology and implement basic knowledge in scientific processes. The following learning objectives had to be reached and supervised by a clinician or physicist, experienced in research methodology:

1. Preparation of a protocol with introduction, objectives and hypotheses, materials and methods sections describing the study and data collection and data sources as well as considerations concerning statistical analyses
2. Collection and processing of data in collaboration with the supervisor
3. Submission and acceptance of an abstract at an international congress.

Long-term objective:
4. Joint preparation of an article together with the supervisor based on the processed results; either as a stand-alone or part of a scientific paper.

KICK OFF AND ORGANISATION

To advertise the project and create a forum where RTTs and experienced researchers had the possibility to present, promote, discuss and network ideas for research projects, an open meeting was arranged.

A short application describing the idea and rationale of each project had to be submitted and we

ANNETTE BOEJEN  MAI-BRITT ELLEGAARD  CAI GRAU
received eight motivation driven applications. Most of the candidates had contact with a scientist to act as a supervisor and all projects were included in the course.

The course took place one day per week for one and a half years. Formalised education by external experts was organised alongside the development of a protocol as the first part of the course; later, the group only met once a month. The project-based learning to prepare the project, collect and analyse data, and prepare performance and presentation (abstract writing) was carried out based on the individual projects and in collaboration with one or more scientists. Assistance for statistical calculations and layouts were offered by the clinical research coordinator.

The course finished with an oral poster presentation in English, validated by an external foreign examiner and followed by an official reception and presentation of diplomas.

**FUNDING AND MANAGEMENT**

The course was a local initiative with financial support for external lectures from the hospital, cost-free academic guidance provided by the clinical researchers, and leave granted one day per week for participants, and only open for participants at the clinic in Aarhus. Management was done by the three of us with Annette Boejen, head of the learning center and Mai-Britt Ellegaard clinical research coordinator as daily leaders and Cai Grau, professor in radiation therapy as supervisor. Clinical leaders participated as a steering group.

**RESULTS**

Seven participants in the group succeeded with international presentations [1-7]:

- One poster, ESTRO 31, Barcelona 2012
- Two posters, 2nd ESTRO Forum, Geneva 2013
- Two oral presentations, 2nd forum ESTRO, Geneva 2013
- One poster, ECCO 2013, Amsterdam
- One poster presentation, ESTRO 33, Vienna 2014.

One of the participants had an early presentation because of maternity leave and another was delayed by dedicated tasks in starting a new unit. One of the participants had to leave the course for personal reasons.

In addition to the learning process, some of the results have already impacted on the further development and implementation of new clinical modalities; e.g. data from “Match at ITV for daily

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<th>PREPARATION OF PROTOCOL</th>
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- Education and exercises:
  - Literature search and RefWorks
  - Basic biostatistics and spreadsheets
  - Clinical epidemiology (design and bias)
  - Questionnaires - possibilities and limitations
  - Presentation skills (posters, use of PowerPoint)

- Education and exercises:
  - Meeting with the group once a month, presentation of own project and articles used in the project

- Education and exercises:
  - Presentation skills (poster, using PowerPoint, English professional language)
  - Meeting with the group once a month, presentation of own project and articles used in the project

Fig. 1 Organisation of education, training and individual projects
on-line radiotherapy for lung cancer”, along with other scientific results, were important for the decision of implementing adaptive strategies in the treatment of lung cancers in April 2013.

EVALUATION
Since formal education is designed in a static model, and project-based learning is based on an individual organisation, participants needed or wanted the formal education to take place in different time slots. The learning strategy was developed during the course. Despite the individual process, collaboration with a group of supervisors and development of the learning strategy, all participants reached their aim and obtained satisfying results. For some of the participants the process is still ongoing. Up to now, results from one project have been included in a scientific article [8].

ACKNOWLEDGEMENTS
We would like to thank all the supervisors and the steering committee for their enthusiastic help, ideas and willingness.

REFERENCES
7. U. Harrow, M.S. Thomsen Fledelius W, Poulsen PR. Inter- and intra-fraction geometric errors in daily image guided radiotherapy of breast cancer patients. PO-0966, ESTRO 31 Barcelona – Spain 2012.
RADIOBIOLOGY
Dear Radiobiology Corner reader,

This month our focus is on DNA repair. We present a meeting report from the DNA repair session of the Association of Radiation Research meeting held at the University of Sussex, UK, in June/July 2014. This excellent meeting was organised by Professor Penny Jeggo and her committee, and the DNA repair session was outstanding with an inspiring keynote speech from Professor Steve Jackson of the University of Cambridge, followed by four excellent talks.

We then turn the spotlight onto Dr Vincenzo D'Angiolella, a junior group leader at the CRUK/MRC Oxford Institute for Radiation Oncology, who tells us about his exciting work on ubiquitin-mediated proteolysis in cell cycle control and regulation of nucleotide production.

Finally, four post-doctoral fellows from Anne’s group present recent papers of relevance to the DNA damage signalling response and double-strand break repair, which reflect the depth and diversity of recent studies.

We would also draw your attention to a further paper in the ‘Read it before your patients’ section, namely “A three-stage genome-wide association study identifies a susceptibility locus for late radiotherapy toxicity at 2q24.1” on p 41 by Fachal et al in Nature Genetics, supporting the role of genetic variants in the development of radiation-induced toxicity.

We hope you enjoy reading this section.

Anne Kiltie, Conchita Vens, Martin Pruschy
The first session in this year’s Association for Radiation Research (ARR) meeting was an excellent collection of talks on DNA repair and chromatin changes.

**Cellular responses to ionising radiation with a 20/20 vision**  
*Stephen P Jackson, University of Cambridge, UK*

Steve Jackson opened the session with a keynote address and an intriguing title. He explained that he proposed this title because he had been working in the field for 20 years and was hopeful that he still had another 20 years to go, so his talk both covered the history of the field and ideas for future work.

Steve started with an overview of the DNA damage response (DDR) in the context of chromatin and the DNA replisome, describing homologous recombination, non-homologous end-joining (NHEJ) and alternative non-homologous end-joining (A-NHEJ) pathways, before going on to describe the history of NHEJ, including the major contributions made by members of his group and by Professor Penny Jeggo, the organiser of the meeting. This included the discovery of Ku and DNA-PK, the three independent DDR systems involving ATM, ATR and DNA-PK, and the identification of other NHEJ components, including XLF/Cernunnos, at a time of great competition in the field. Although the list of NHEJ components was thought to be complete, Steve presented exciting, as yet unpublished data on a recently discovered novel component of the NHEJ pathway.

Steve then argued that, having assembled the necessary toolkit, the field is only just getting going, and he went on to consider the next 20 years, presenting us with some major themes for exploration. These included the communication between pathway proteins, regulation by post-translational modifications, and sequential assembly and disassembly of protein complexes, highlighting new examples that his lab had identified. He explained how increased understanding of the underlying mechanisms could explain their functional connections to disease states and how these might be exploited clinically. Post-translational modifications including phosphorylation, acetylation, deacetylation, histone modification, ubiquitylation and poly(ARP)ribosylation provide many druggable targets, allowing exploitation of synthetic lethality and other anti-cancer therapeutic opportunities.
Pathways of double strand break repair during the mammalian cell cycle
Markus Lobrich, University of Darmstadt
Darmstadt, Germany

Markus Lobrich followed with his talk on double strand break (DSB) repair pathways during the cell cycle. He presented his experimental system, where asynchronous cells are marked in S-phase by EdU and in G2 by CENPF, allowing identification of cells in G1, S and G2 phases of the cell cycle and scoring of gamma-H2AX foci in a cell cycle-specific manner.

Having set the scene by explaining the biphasic nature of DSB repair, and also differential repair in euchromatin (using NHEJ in both G1 and G2) and heterochromatin (observed as the slow repair component, using HR in G2), Markus then posed his key experimental question: What is the slow component in G1 phase? It is known that CtIP initiates DSB resection in G2, to promote HR, but CtIP also functions in NHEJ during G1, although the mechanism underlying activation of CtIP in G1 was unknown. Markus’s group identified Polo-like kinase 3 (PLK3) as phosphorylating CtIP at S327 and T847 in a damage-inducible manner. Markus elegantly explained this work, and demonstrated that complex DSB produced by carbon ions and alpha particles are those which require PLK3 and CtIP for resection in G1.

A novel BRCA1 associated mRNA splicing complex required for efficient DNA repair and maintenance of genomic stability
Kienan Savage, Queen’s University
Belfast, UK

In the third talk, Kienan Savage set the scene by explaining the role of BRCA1 mutations in inherited breast and ovarian cancers and also the multiple different functional complexes of which BRCA1 is a component. BRCA1 is phosphorylated by different kinases, such as ATM and ATR, resulting in different functional effects. Kienan asked the question: How do phosphorylation events mediate the formation of different complexes?

Using a peptide pulldown assay to either phosphorylated or non-phosphorylated proteins, Kienan’s group identified BCLAF1 in phosphorylated BRCA1 pulldowns, and found it to interact with BRCA1 in response to a range of DNA damages. The BRCA1/BCLAF1 interaction mediates formation of a complex containing BRCA1 and the mRNA splicing machinery and, although not directly involved in DNA repair processes, BCLAF1 is required for DNA repair and genomic stability. Kienan explained that BRCA1 sits on the promoters of 1000’s of genes and regulates their expression in response to different types of stress, and then BCLAF1 is recruited to a subset of gene promoters in a BRCA1-dependent man-ner. He then demonstrated the effects on mRNA splicing and protein expression in a series of experiments based on three model genes, resulting in effects on the cellular response to DNA damage.
Insights into ribonucleotide reductase (RNR) regulation during cell cycle progression and DNA damage response

Vincenzo D’Angiolella, University of Oxford
Oxford, UK

In the first of two short talks, Vincenzo D’Angiolella presented his work on ribonucleotide reductase, which catalyses the conversion of ribonucleotides to deoxyribonucleosides, required for DNA synthesis. He explained that this is an important enzyme, as it is the target of chemotherapeutic agents including gemcitabine, clofarabine, 5FU, permotrexed and methotrexate. Cyclin F, an E3 ubiquitin ligase, is involved in the regulation of RRM2 (Ribonucleotide Reductase family Member 2), and effects its degradation during G2. Vincenzo’s group found that, after DNA damage, cyclin F is down-regulated in an ATR-dependent manner to permit accumulation of RRM2. If cyclin F is not removed effectively, then DNA repair is delayed and the cells are sensitised to DNA damage. Vincenzo is examining the mechanisms in more detail, but work so far underscores the relevance of dNTP pool homeostasis in genome stability and DNA repair.

BAF180 promotes cohesion and prevents genome instability and aneuploidy

Peter M Brownlee, University of Sussex
Falmer, UK

In the final talk, Peter Brownlee discussed BAF180, a subunit of the PBAF chromatin remodelling complex required for establishing sister chromatid cohesion, which is mutated in 41% of renal cancers and 17% of intrahepatic cholangiocarcinomas. Peter hypothesised that BAF180 may prevent tumourigenesis by promoting cohesion. He presented a series of experiments in BAF/- mouse embryonic stem cells, in 1BR-hTERT cells depleted of BAF180 and human tumour samples, and showed that there was reduced centromeric cohesion, increased micronucleus formation and abnormal anaphases, with increased DNA damage sensitivity and dynamic chromosomal instability following DNA damage. These findings may provide a mechanism for BAF180’s tumour suppressor activity.
SPOTLIGHT

Dr Vincenzo D’Angiolella

Cancer Research UK and Medical Research Council Oxford Institute for Radiation Oncology
Department of Oncology
University of Oxford
Oxford, UK

Biography

Vincenzo D’Angiolella is an MRC junior group leader at the CRUK/MRC Oxford Institute for Radiation Oncology within the University of Oxford. His team is composed of four people, one postdoc and two DPhil candidate students.

Furthermore, Dr Annalisa Carlucci recently joined the team as a visiting scientist after being awarded an international fellowship (UICC).

Vincenzo obtained his Medical Degree (MD) from the University of Naples “Federico II” in Italy in 2002, and subsequently practised internal medicine to obtain his medical licence. Although fascinated by the fields of cardiology and radiology, he realised that his real passion was to pursue a scientific career. Therefore, he also completed a PhD at the same university. During his PhD studies, Vincenzo was introduced to cell cycle research and used *Xenopus Laevis* to study the basic mechanisms of cell cycle progression. These studies further enforced his passion for science and following the completion of his studies, he accepted a post as a postdoctoral fellow at the New York University (NYU) School of Medicine in New York, USA, at the laboratory of Dr Michele Pagano, where he continued his research in the cell cycle field and extended his studies to a more general role of ubiquitin-mediated proteolysis in multiple aspects of cell biology.

Vincenzo has recently established his own laboratory in Oxford and is currently focussing on the mechanisms of ubiquitin-mediated proteolysis that regulate cell growth and cancer cell survival. The human genome codes for approximately 500 E3 ubiquitin ligases and their role is poorly understood. The study of these enzymes might prove useful in developing new therapies that specifically target their mechanism of action.

Vincenzo also identified a novel pathway that regulates production of deoxyribonucleotides (dNTPs), the precursors of DNA synthesis during the cell cycle. Many compounds targeting nucleotide production are currently used in cancer therapy (i.e. gemcitabine, hydroxyurea, clofarabine, 6-thioguanaine, and 5-FU). Identification of new pathways that regulate dNTP production might provide insights into drug resistance, predict response to chemotherapy, and prove to be powerful tools for the design and implementation of new therapies. Using unbiased “state-of-the-art” proteomic and genetic screens, the lab has identified novel genes that regulate cell survival in both nucleotide homeostasis and ubiquitin-mediated proteolysis. Exciting times lie ahead in unravelling the function of the orphan genes identified and their roles in cancer pathogenesis.
Vincenzo was awarded fellowships from AIRC (Associazione Italiana per la Ricerca sul Cancro) and AICF (American Italian Cancer Foundation), and was a Scholar of the Leukemia & Lymphoma Society from 2008 to 2011. He has authored or co-authored several publications in major scientific journals (e.g., Nature and Cell).

**Vincenzo explains his research in more depth**

“In each cell division cycle, cells replicate their DNA (in S-phase) and distribute the genetic information equally to the daughter cells (in M-phase). Cell cycle phases are driven by the periodic activity of cyclin dependent kinases (CDKs), which in turn is controlled by the oscillations of the cyclins, the obligate CDK cofactors. CDK activity drives cell cycle phase transitions in a very accurate and ordered manner, and these transitions can be blocked by multiple checkpoint mechanisms that monitor each phase for completion and fidelity. During cell cycle transitions and checkpoints, rapid elimination of target proteins is controlled by ubiquitin-mediated proteolysis. The polyubiquitin chain is assembled on the substrate protein via an enzymatic cascade, in which ubiquitin is activated by a covalent linkage to an E1 ubiquitin activating enzyme and transferred to an E2 ubiquitin conjugating enzyme. The E3 ubiquitin ligases mediate the transfer to a lysine residue in the substrate from the E2 ubiquitin conjugating enzyme. Notably, the ultimate regulation of the reaction is dictated by the E3, which determines substrate specificity. The irreversible nature of ubiquitin-mediated proteolysis allows controlled state transitions. The ubiquitin system is used in a variety of biological responses and approximately 500 ubiquitin ligases have been identified in the human genome. The orchestrated action of ubiquitination and proteolysis ensures the correct execution of the cell cycle and coordinates the proper response to exogenous stimuli. Alteration of the mechanisms monitoring cell cycle progression leads to cancer whereby cell proliferation is not integrated with checkpoint control signals. Instead cancer cells tend to proliferate in an uncontrolled fashion and become insensitive to the checkpoint signalling that ensures accurate replication of DNA and distribution of the genetic material to the daughter cells during mitosis.

“During my postdoctoral studies, I investigated the function of cyclin F. Cyclin F (also known as Fbxo1) is the founding member (and namesake) of the F-box protein family of E3 ubiquitin ligases. Cyclin F prevents genome instability by restricting the production of dNTPs to S-phase, where dNTPs are required for DNA replication. Cyclin F ubiquitinates the Ribonucleotide Reductase family Member 2 (RRM2), a subunit of Ribonucleotide Reductase (RNR). RNR catalyzes the conversion of ribonucleotides to dNTPs, which are used in the synthesis of DNA during replication and repair. We found that the nuclear pool of cyclin F controls the degradation of RRM2 during the G2-phase of the cell cycle. The regulation of RRM2 by cyclin F is required to maintain balanced levels of dNTPs. Failure to regulate dNTP levels properly causes genome instability and a hypermutator phenotype. Since dNTPs are also required for DNA repair synthesis, cyclin F levels drop drastically after DNA damage, coincident with the accumulation of RRM2. The degradation of cyclin F after DNA damage is necessary to allow the accumulation of RRM2 within the nucleus to allow dNTP production for DNA repair.

“RNR is the target of many anti-cancer drugs (i.e. gemcitabine, hydroxyurea, clodarabine) used currently in the treatment of non-small cell lung cancer, pancreatic cancer, bladder cancer, and breast cancer. Inhibition of RNR is known to sensitize cancer cells to genotoxic stress. We are currently investigating the mechanisms that regulate cyclin F-RRM2 axis and dNTP production during cell cycle and checkpoint response. Genetic evidence from yeast suggests that the regulation of dNTP pools is essential for the correct execution of the DNA damage checkpoint response. We are thus investigating the crosstalk between RNR and checkpoints in mammalian cells in more detail. Our initial findings of cyclin F-RRM2 axis extend to a broader role of dNTP production in cell cycle homeostasis and checkpoint response. Identification of new pathways that regulate RNR and dNTP production upon..."
genotoxic stress might shed light into drug resistance, predict response to therapy and lead to the design and implementation of new therapies (inhibitors of the checkpoint regulators, e.g. chk1, ATR, ATM).

“In addition to cyclin F, numerous other F-box proteins are coded by the human genome. We have used an siRNA screen to identify genes that are involved in cell cycle and cell survival. We have recently identified a novel E3 ligase that regulates cell survival through the control of Sonic Hedgehog (SHH) pathway. Since SHH pathway inhibitors are being studied in clinical trials, we would like to unravel the role of this protein in vivo and extend these findings to the crosstalk between SHH and ionising radiation.

**Conclusions**

“Establishing a new laboratory comes with numerous challenges, but it also opens the long-sought opportunity to explore novel routes of investigation. I feel highly excited about the opportunities that lie ahead and I believe strongly that advancements in biology will provide a totally novel view of classical medicine in the near future. Although current studies have defined the molecular alterations in many human tumours, more studies are necessary to define the basic mechanisms of cell survival. In order to apply targeted therapy effectively, we will need to identify node components of signalling pathways. I am confident that we will see great progress through a combination of basic and translational research and I hope that our efforts in the laboratory research will translate into improved treatment of cancer.”
Phosphorylation of EXO1 by CDKs 1 and 2 regulates DNA end resection and repair pathway choice

Tomimatsu et al.
Paper review by Dr Eva McGrowder

SETD2-Dependent Histone H3K36 Trimethylation is Required for Homologous Recombination Repair and Genome Stability

Pfister et al.
Paper review by Dr Blaz Groselj

UBR5-mediated ubiquitination of ATMIN is required for ionizing radiation-induced ATM signalling and function

*Proc Natl Acad Sci U S A.* 2014;111(33):12091-6
Zhang et al.
Paper review by Dr Judith Nicholson

RPA antagonizes microhomology-mediated repair of DNA double-strand breaks

*Nat Struct Mol Biol.* 2014;21(4):405-414
Deng et al.
Paper review by Dr Martin Kerr
PHOSPHORYLATION OF EXO1 BY CDKS 1 AND 2 REGULATES DNA END RESECTION AND REPAIR PATHWAY CHOICE

Tomimatsu et al.

DNA double-strand breaks (DSBs) pose a potential threat to the integrity of our genome. Non-homologous end-joining (NHEJ) and homologous recombination (HR) are the two main pathways to counter this threat. The activity of these pathways is tightly regulated throughout the phases of the cell cycle, whereby NHEJ is predominant during G1 whilst HR is restricted to late S/G2 phases of the cell cycle. Cell cycle-mediated mechanisms of regulating the switch between NHEJ and HR are not well understood. DNA end resection can serve as that switch in determining repair pathway choice, whereby resection would favour HR whilst impeding NHEJ. Resection is a two-step process comprising short-range and long-range resection and cell cycle regulators cyclin-dependent kinases (CDKs) have previously been shown to play a role in the initial step of resection through modulation of C-terminal binding protein-interacting protein (CtIP) and Nbs1. Now however, Tomimatsu et al. describe a novel mechanism by which CDKs regulate repair pathway choice through phosphorylation of EXO1, a long-range resection nuclease. The authors found that EXO1 was phosphorylated at four carboxy-terminal serine/threonine sites by CDKs 1 and 2 as the cells progressed through S and G2 phases of the cell cycle. In fact, phosphorylation was observed as early as G1 and increased as the cells progressed through to S and G2 phases. The authors were able to generate phospho-specific antibodies against one of these sites and thus went on to demonstrate that EXO1 was directly phosphorylated at this site in a cell cycle- and CDK-dependent manner. They also found that phosphorylation of EXO1 promoted DNA end resection, in part, through increased recruitment of EXO1 at sites of DSBs. The HR repair pathway was attenuated, while the NHEJ pathway was augmented upon mutation of these phosphorylation sites. Furthermore, the authors also observed that mutation of all four sites or each individually resulted in reduced association of EXO1 with BRCA1. This study further strengthens the link between cell cycle regulation and its impact on repair pathway choice. Furthermore, these findings raise questions worthy of further investigation. For instance, it would be interesting to know the impact of EXO1 phosphorylation on the resection-dependent alternative non-homologous end-joining pathway, which is also functional to some extent during the phases of the cell cycle, particularly during S phase.
SETD2-DEPENDENT HISTONE H3K36 TRIMETHYLATION IS REQUIRED FOR HOMOLOGOUS RECOMBINATION REPAIR AND GENOME STABILITY

Pfister et al.  

The DNA double-strand break (DSB) is the most lethal form of DNA damage if left unrepaired. It also contributes to genome instability, if repaired inaccurately, such as occurs via microhomology-mediated end-joining (MMEJ). One of the most important and error-free DSB repair pathways is homologous recombination (HR). In eukaryotes DNA is wrapped around histone proteins forming the basic unit called the nucleosome. Post-translational modifications of the nucleosome histone tails (e.g. lysine (K) methylation) have an important role in facilitating DSB repair and accessibility of various factors to the chromatin. Trimethylation of H3K36 (H3K36me3) is catalysed by the methyltransferase SETD2 and is associated with transcription elongation. SETD2 is a tumour suppressor and mutations of SETD2 have been found in breast, lung and several other cancer types.

In a recent study published in Cell Reports, Pfister et al. investigated the role of SETD2-dependent H3K36me3 in HR repair. SETD2 depletion sensitised the cells to DNA damaging agents such as mitomycin C, camptothecin and ionizing radiation. They also observed reduced use of HR, accompanied by an increased use of the error-prone MMEJ pathway in cells depleted of SETD2 or of the major HR protein, RAD51. Recruitment of the major HR proteins RAD51 and RPA to the DSB sites was significantly reduced, indicating the presynaptic role of SETD2 protein. Abolishing the H3K36me3 mark without affecting SETD2 also reduced HR, suggesting that this histone modification is required for accurate DNA repair by HR and maintenance of genome stability.
The cellular DNA damage response to double-strand breaks induced by ionising radiation is activated as the Mre11/Rad50/Nbs1 (MRN) complex binds to ATM via the Nbs1 subunit. This leads to phosphorylation of ATM substrates including p53 and SMC1, which initiates the formation of DNA repair foci and activates the cellular response to DNA damage. Recently ATM interacting protein (ATMIN) has been identified as a cofactor which activates ATM after hypotonic stress, but not ionising radiation, suggesting an additional regulation mechanism for ATM.

Zhang et al. have demonstrated that Nbs1 and ATMIN compete for binding to ATM. This is regulated by the E3 ligase UBR5 which binds to and ubiquitinates ATMIN, which inhibits the ATMIN-ATM interaction. The authors map a conserved ubiquitination site in ATMIN, and show that ATMIN ubiquitination allows an increase in the ATM-Nbs1 interaction leading to activation of ATM. UBR5 ubiquitination of ATMIN is stimulated by ionising radiation, and loss of UBR5 or mutation of the conserved ubiquitination site both abrogate ATM signalling and G2/M checkpoint activation after ionising radiation. This indicates that ATMIN ubiquitination is an important step in the initiation of the DNA damage response as it allows MRN mediated activation of ATM to proceed. The authors also show that UBR5 downregulation in the absence of ATMIN does not attenuate phosphorylation of ATM substrates, indicating that the main role of UBR5 in regulating the DNA damage response is via ATMIN.

A model is proposed in the paper in which ubiquitinated ATMIN dissociates from ATM, allowing the binding of ubiquitinated Nbs1 to activate ATM signalling. As Nbs1 is also ubiquitinated by the E3 ligase Skp2 upon DNA damage this represents a new mechanism controlling DNA repair which is mediated by increased ubiquitination of two ATM regulators as a post-translational signalling modification.
Cells have evolved to repair DNA double-strand breaks (DSB) in a number of ways. Homologous recombination (HR) is an error-free mechanism whereby a sister chromatid is utilised as a template for repair. Non-homologous end joining (NHEJ), on the other hand, involves direct ligation of broken DNA ends; a process that is dependent on the Ku proteins and Ligase IV. A third mechanism for repair, termed microhomology-mediated end-joining (MMEJ), also involves direct ligation of DNA ends, but in a manner independent of Ku and Ligase IV. MMEJ instead relies on DNA end resection to expose regions of microhomology on opposing single stranded DNA (ssDNA) that allow the strands to anneal. This process is highly mutagenic and can often result in chromosome rearrangements.

In a recent study published in *Nature Structural & Molecular Biology*, Deng *et al* developed a chromosomal end-joining assay in *S. cerevisiae* to examine the requirement for end resection and strand annealing during MMEJ. The authors also found that whilst resection was able to influence the ability to expose microhomologies in DNA, it was not limiting. Furthermore, yeast carrying a hypomorphic mutation in *rfa-1* (the yeast orthologue of *RPA1*) had up to a 350-fold increased frequency of MMEJ. The RPA complex coats ssDNA after resection and is subsequently exchanged for Rad51 through the Rad52 mediator, to allow for homologous strand invasion in HR. However, yeast mutants in *rad51* and *rad52* only exhibited 3- to 6-fold increase in MMEJ, suggesting that the increase in MMEJ in the *rfa-1* mutants is not simply due to defective HR. The authors went on to show that the frequency of MMEJ in *rad51/rfa-1* and *rad52/rfa-1* double mutants was significantly elevated compared to the *rfa-1* single mutant, further indicating that RPA has an independent role to Rad51 and Rad52 in suppression of MMEJ.

The proposed model is that the RPA complex coats ssDNA to inhibit spontaneous annealing of microhomologies and is a critical determinant for repair by MMEJ in yeast. It remains to be elucidated if RPA plays a similar role in preventing MMEJ in mammalian cells.
In the rapidly evolving field of science and radiation oncology, the ESTRO School offers an ideal platform to follow Continuing Medical Education (CME) courses. Just have a look at our 2015 programme and you will be convinced. Among the 35 live courses on offer, three are totally new and in this issue, we introduce the course directors, Lena Specht, Ursula Nestle and Ben Heijmen (physics corner). They will tell us more about what to expect from these new ESTRO CME courses, but also why it is important to foster education in haematological malignancies, molecular imaging in radiation oncology and to create a research masterclass in radiotherapy physics. For more information, the 2015 guide has already been sent by postal mail to our members. If you haven’t received it, you can check it out on our website.

Pride of place will be given to educational activities at the 3rd ESTRO Forum which will take place 24 - 28 April in Barcelona: five pre-meeting courses, eight contouring workshops and three tumour board sessions. Consult our full programme and updates online and don’t forget that you have a discount on all our courses, live and online, if you are an ESTRO member for 2015.

Finally, we are pleased to inform you that it was decided at the June strategy retreat (JSR) that the function of the Education and Training Committee of ESTRO would be expanded. As the role of this committee will continue to evolve and reinforce education as one of the three supporting pillars of the Society’s mission, it will become an ESTRO Education Council.
Educational collaboration between ESTRO and the Royal Australian and New Zealand College of Radiologists (RANZCR), Faculty of Radiation Oncology.

In late 2012, the Royal Australian and New Zealand College of Radiologists (RANZCR), Faculty of Radiation Oncology signed a Memorandum of Understanding (MoU) with ESTRO about some early scientific and educational collaborations. As part of this arrangement, all 160 trainees within the Australian and New Zealand training programme became automatic affiliate members of ESTRO.

Sandra Turner and Ben Hindson are the organisers of these ESTRO RANZCR online workshops dedicated to our colleagues from “Down Under”. On the next page, they tell us about the importance of this collaboration and its future developments.

Interview with Associate Professor Sandra Turner and Dr Benjamin Hindson

Online delineation workshops on head and neck cancer

Three sessions on 9, 15 & 22 December 2014
What is the added value of the ESTRO Fellowship in Anatomic deLineation and CONtouring (FALCON) delineation workshops for RANZCR?

One of the key practical educational benefits of this collaboration from our perspective was greater access to FALCON teaching opportunities for our trainees. In a major reform of our radiation oncology curriculum and training programme, implemented in 2009, the need to increase formalised learning and feedback in the area of technical planning skills and contouring was identified. ESTRO was already well advanced in its FALCON program and many Australian and New Zealand ESTRO members were already taking part in these, especially the live sessions in Europe, with enthusiastic responses.

Facilitating access to the increasing number of FALCON workshops for our members seemed an ideal way to solve this potential gap in radiation oncology training. The ESTRO School was extremely helpful in achieving our aim by agreeing to run on-line FALCON in a time zone suitable for our members. The first of these three-session workshops was held in February/March this year on breast cancer and the second in October on gynae. The technology worked well and the feedback was very positive. We are currently trying to confirm a program of FALCON for other tumour sites over a 12 to 18 month period. We have discussed opening this to participants around the Asia-Pacific region which will likely increase the interest and educational experience for all. The next on-line FALCON directed at this part of the world will hopefully take place in late 2014, with a gynaecology brachytherapy focus.

**FALCON workshops can be conducted live and online and you experienced both. How would RANZCR like to continue with FALCON in the future?**

This year also marks the first live FALCON workshop on rectum cancer held in Australia, in conjunction with the RANZCR Annual Scientific Meeting. This was attended by many trainees and senior radiation oncologists, and allowed some local ‘experts’ to join the teaching faculty. If it continues to be successful, and there is every indication that it will be, RANZCR would hope that similar sessions might run in conjunction with future national annual meetings, depending on ESTRO’s resources.
How was the workshop perceived by the participants?
Trainees were surveyed last year about their perceptions of the ESTRO collaboration and were very keen for this to continue. The large majority had already taken part in a teaching course or FALCON workshop and they were strongly supportive of continuing the automatic arrangement they are currently enjoying. It is likely that as familiarity around the value of these learning tools increases, so will the demand for more such resources.
In preparation for the FALCON workshop held in Melbourne as part of your Annual Scientific Meeting, you, as the Australian meeting convenor, attended the rectal FALCON in Prague in May 2014. How useful was the workshop for you?

In Prague the workshops did not disappoint. We started long before the course with homework and this allowed for great debate and comparison during these practical sessions. I realised that the pre-course work is the key to a successful workshop. Assessing the participants’ volumes identifies the areas of controversy worth discussing and reviewing in the workshop.

Having Professor Vincenzo Valentini lead the Prague workshop was invaluable to the session. The regional experts’ involvement in the course was also very important. In Melbourne, we had the pleasure of Prof Valentini leading our workshop and he was supported by two local ▼
What did the participants enjoy about FALCON?
The FALCON platform is very simple for participants to navigate and use. We are very excited to have all the input and expertise from the FALCON team available in Melbourne this September.

Was the RANZCR FALCON workshop on 5 September different from the workshop in the course you attended in Prague? How?
In Melbourne, we were running two workshops in the one day to maximise the opportunity for our members to take part. Participants were radiation oncologists, radiation therapists and radiation oncology trainees. Overall the workshop was similar to the Prague one and based on prior homework. However, there were some differences based on my experience (albeit limited) as a participant in the European course.

The Melbourne workshop focussed on two cases rather than the three that ESTRO used previously. It was felt that fewer cases would reduce repetition and allow more discussion around controversial areas.

In addition, there are differences in the delineation guidelines used widely in Australia and New Zealand, compared to those developed by ESTRO. Having Prof Vincenzo Valentini and Associate Profs Sam Ngan and Andrew Kneebone on the teaching faculty for this session, highlighted and examined these differences. This area of discussion by the experts and participants was a new and interesting perspective for the Australian workshops. We hope that this added further educational value to what was already a highly valuable ESTRO teaching resource.

The report on the online delineation workshops on gynaecological cancer held in October 2014 will be published in the January-February issue of the newsletter.
This online delineation workshop is aimed at junior clinical or radiation oncologists who wish to improve their contouring skills or at more senior specialists who want to refresh and validate their knowledge and skills in this field.

The workshop will be conducted through three interactive web conference sessions that offer the opportunity to compare delineations from participants and experts and discuss inter-observer variability and the available guidelines.
**WORKSHOP FACULTY**

Workshop Director  
Jesper Eriksen, Radiation Oncologist, Odense University Hospital, Odense, Denmark

Head and Neck Cancer Specialist  
Vincent Grégoire, Radiation Oncologist, Cliniques Universitaires St-Luc, Brussels, Belgium

**WORKSHOP PROGRAMME**

1st session: 18:00-19:00 hrs  
(CET time - Brussels, GMT+01:00)
- Presentation of the programme of the workshop and the methodology
- Presentation of the webex system and how to communicate during the sessions
- Presentation of the teachers and tutors (explanation of their roles) and of the participants
- Presentation of the clinical case
- Presentation of the contouring tool (how to contour, save and submit contours).

Followed by one week of practising from home with contouring exercises.

2nd session: 18:00-20:00 hrs  
(CET time - Brussels, GMT+01:00)
- Guidelines presentation
- Comment and discussion on contours from the first week.

Followed by one week of practising from home with contouring exercises based on the guidelines taught.

3rd session: 18:00-19:30 hrs  
(CET time - Brussels, GMT+01:00)
- Discussion on 1st and 2nd contours
- Comparison with the expert contours.

Followed by one month free web access to this case for participants.

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More information and application form available on line.

Please email your registration to ESTRO to the attention of Miika Palmu, ESTRO project manager at mpalmu@estro.org.

Please note that the number of places is limited to 30 participants, registration will be based on a first-come, first-served basis.
COURSE REPORTS

Biological Basis of Personalised Radiation Oncology  
29 June - 2 July 2014 | Brussels, Belgium

Multidisciplinary Teaching Course in head and neck Cancer  
29 June - 2 July 2014 | Athens, Greece
I would like to thank, on behalf of all of the participants, Professors Kevin Harrington, Martin Pruschy, Jan Alsner, Conchita Vens, Marie-Catherine Vozenin, Daniel Zips and the ESTRO organisers for a highly stimulating and inspiring course on the biological basis of personalised radiation oncology. The four-day course was held at the ESTRO head office in Brussels and featured an international multidisciplinary audience of radiation oncologists, biologists and physicists from as far afield as India and Australia.

The broad scope of the course included genetics, cell signalling, stem cells, angiogenesis, metabolism, metastasis, normal tissue responses, immune responses and functional imaging. One of the first lectures linked the ‘5 Rs of radiobiology’ to the ‘hallmarks of cancer’. As a physicist, ▼
with training in classical and quantitative radiobiology, I found this particularly helpful. Many of the talks included case studies, highlighting how the molecular biology concepts covered relate to the patients treated at our institutions. Tutorials were interspersed throughout the lectures, giving participants a chance to consolidate what they had learned and present their answers to problems posed to the rest of the group.

The course was delivered in a friendly, informal manner, which allowed for ample discussion around the topics covered. The passion and enthusiasm of the faculty for their areas of expertise were apparent, particularly when discussing promising new approaches to combining biologically targeted therapies, such as cell cycle checkpoint inhibitors or immune therapies, with radiation.

Brussels provided participants with an opportunity to enjoy impressive architecture and wash down waffles and chocolate with some of the 450 or so different Belgian beers. I would highly recommend this course to those interested in understanding the biological basis of radiotherapy, and strategies to exploit those biological processes to improve patient outcomes.

Jamie Dean
PhD student
The Institute of Cancer Research
London, UK
jamie.dean@icr.ac.uk
Having moved jobs at the start of the year and taken on head and neck oncology as a new site sub-specialty I quickly looked for a training course to boost and update my knowledge. I found the ESTRO Multidisciplinary Teaching Course in Head and Neck Cancer - an added bonus was the location: Athens. This was the second ESTRO teaching course that I have attended, and it more than matched my expectations.

The teaching faculty was certainly multidisciplinary with three radiation/clinical oncologists, two medical oncologists, two surgeons, and a radiologist which ensured balanced content. The course timetable was full without being overwhelming and covered the main topics in head and neck oncology. We started with some introductory lectures then a standard structure was used which presented the current evidence for...
each topic from the key disciplines followed by a clinical case discussion session. The atmosphere was friendly and open which encouraged questions from and discussion with the audience. This format and the fairly small size of the course enabled in-depth discussion and questions, in particular around where the evidence base did not match real clinical cases, and these discussions often continued during the coffee breaks.

Prior to the course we were given some homework which consisted of a clinical case with imaging and interactions to outline the treatment volumes and certain specific organs at risk. This was partly an exercise in following the nodal consensus guidelines but also the selection of target regions, and the discussion of this was very useful.

The participants were somewhat less multidisciplinary than the faculty, with the vast majority of them being radiation or clinical oncologists (i.e. dual trained in radiotherapy and chemotherapy) - mainly senior trainees or junior consultants. For me it was the perfect level and I think it would benefit senior trainees, new consultants or oncologists with a fairly general practice or those who want an update on the topic.

Athens at the end of June was lovely and very warm with blue skies and sunshine. The Royal Olympic Hotel was comfortable and included a lovely roof terrace for meals with a fantastic view of The Acropolis and the Temple of Zeus. The hotel was in a perfect location to make the most of our free time in the evenings close to Athens’ famous monuments, restaurants, and markets. The course dinner was extremely pleasant and a great opportunity to get to know fellow oncologists, not to mention to sample some Greek wine. I hope to keep in touch with some of the new oncology friends I have made and continue building on my new knowledge.

Kate Cardale
Consultant Clinical Oncologist
St James’ Institute of Oncology
Leeds Teaching Hospitals NHS Trust
Leeds, UK
Research masterclass in radiotherapy physics:
Read the interview with Ben Heijmen, Course
director in the Physics Corner on p 59

3 - 6 September 2015 | Prague, Czech Republic

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Haematological Malignancies

In collaboration with ILROG
(International Lymphoma Radiation Oncology Group)
3 - 5 September 2015 | London, United Kingdom

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ESTRO/EANM Course on Molecular Imaging and Radiation Oncology

22 - 25 February 2015 | Madrid, Spain
Why was this course created?

Molecular imaging (MI) has definitely arrived in radiation oncology. PET imaging is now routinely applied for many indications, and MRI is increasingly performed with functional sequences (fMRI). Radiation oncologists and imaging professionals need to work together to understand and implement the added value of these techniques when making treatment decisions. Therefore, this course was created as an extended update of the well-received former “ESTRO/EANM seminar on PET in radiation oncology”. Beyond PET based gross tumour volume (GTV)-delineation, we have an increasing need to learn about MI methods for treatment selection, sub-volume definition and response evaluation. This advanced course, again jointly organised by ESTRO and EANM, aims at providing the participants...
profound knowledge and skills in order to deal with the challenges associated with the use of MI methods in all fields of radiation oncology. As a new feature, the course will – beyond PET – also address some aspects of molecular MRI.

**What are the main learning outcomes?**

This course will be highly interdisciplinary and interactive – including group work and hands-on workshops. We will provide the participants with advanced knowledge on the current evidence of MI in staging, treatment planning and response assessment of the main solid tumours. They will understand the technical issues of PET and fMRI in radiotherapy treatment planning, learn to handle the technical challenges of MI-based GTV delineation and gain practical experience in the diagnostic background of nodal clinical target volume (CTV) concepts. We hope that the participants will also take home some interesting questions for future research in this field.

**How did you select the teachers?**

The faculty will be international with seven teachers coming from The Netherlands, Finland, Italy, France, Germany and the UK. Most of the teachers have already taught on previous PET course and/or at other ESTRO courses. All of them have been actively involved with MI in radiation oncology for years, both in clinical care and research. We have selected a faculty covering all the main oncologic fields, contributing practical experience in radiation oncology, nuclear medicine and radiology. Physics topics on PET, MRI and radiation oncology will also be covered in depth.

Beyond the lectures and guidance of interactive hands-on sessions in small groups, the group of teachers will be present throughout the course and contribute their complementary knowledge in the morning plenary discussions on the results of the group work.

**Who should attend?**

We would be happy to welcome anyone who is interested. This may be a senior resident or a young specialist either in radiation oncology, nuclear medicine or radiology, but also researchers or radiation therapists (RTTs), who intend to expand their knowledge and skills in the use of MI methods for radiation oncology. All these individuals may well benefit from this course.
INTRODUCTION

E-LEARNING

COURSE REPORTS

2015 NEW COURSES

ESTRO FELLOW

HAEMATOLOGICAL MALIGNANCIES

In collaboration with ILROG (International Lymphoma Radiation Oncology Group)

3 - 5 September 2015
London, United Kingdom

INTERVIEW WITH THE COURSE DIRECTOR:

Lena Specht
Clinical Oncologist
Rigshospitalet
Copenhagen, Denmark

Why was this course created?

Haematological malignancies constitute a complex group of diseases. In particular, the new lymphoma classification has defined more than 60 lymphoma disease entities, each of which may be localised to any part of the body or be widely disseminated. Most of these diseases are highly radiosensitive, and effective systemic treatments are also available. Radiotherapy is an important part of the treatment; in some situations as the only treatment modality, in other situations as part of multimodality treatment.

The introduction of modern 3D planning and highly conformal treatment techniques combined with advanced imaging has enabled a much more individualised treatment with irradiation, leading to highly significant reductions in normal
tissue irradiation compared to the large radiation fields of the past, which should no longer be used.

Radiation oncologists treating patients with haematological malignancies must have a thorough knowledge of the many different disease entities and the role of radiotherapy in the multimodality treatment of each of them. A large proportion of these patients become long-term survivors, and target volumes and radiation doses must be limited to what is absolutely necessary in order to minimise the risk of long-term complications. Special techniques must be used for certain clinical presentations to further reduce long-term risks.

This course was created to teach the new principles and practice in radiotherapy for haematological malignancies. It is carried out in collaboration with the International Lymphoma Radiation Oncology Group (ILROG), a worldwide organisation of radiation oncologists specialising in the treatment of lymphomas. This organisation has recently published guidelines for modern radiotherapy of lymphomas, which have been adopted by most international groups.

**What are the main learning outcomes?**

By the end of this course the participants should be able to design strategies for the multimodality treatment of haematological malignancies. They should be able to apply modern principles for radiotherapy and to define target volumes and prescribe radiation doses and fractionation schedules appropriate for different disease entities and clinical situations. They should be able to apply and evaluate different treatment techniques depending on disease localisations and risks of normal tissue complications.

**How did you select the teachers?**

Teachers were selected from among clinical and radiation oncologists with a strong record of clinical practice and research in haematological malignancies, mostly from Europe, and mostly active members of ESTRO and ILROG. Most of the teachers have been involved in the development of the new guidelines for lymphoma radiotherapy. Specialists from other specialities involved in the multimodality treatment of haematological malignancies, e.g., medical oncology/haematology, pathology and imaging, are also involved.

**Who should attend?**

Radiation oncologists who are or intend to become involved in the treatment of haematological malignancies.
You have been involved with the ESTRO Fellow programme since the early stages when it was created in 2011 at the 30th ESTRO Anniversary. Why did you believe in this project from the beginning?
I feel that it is the responsibility of the senior ESTRO members and councils to ensure that there is a natural evolution and development of junior members to eventually take over the running of the Society. For this to happen, we need to involve as many members as possible in Society activities so that they can learn about the ESTRO philosophy and policy and that they can eventually assume increasing responsibility for the activities of the Society. The ESTRO Fellow programme is intended to facilitate this process.

Why would you encourage your young colleagues to participate in the ESTRO Fellow programme?
For any European (and many non-European) radiation oncology professional, ESTRO is the main forum for education, networking and exchange of scientific and clinical information. Being appointed as an ESTRO Fellow demonstrates professional competence and a commitment to the Society and should facilitate involvement in Society affairs. Active participation in the Society creates many career opportunities and raises the profile of the individual, as well as giving them satisfaction of knowing they are contributing towards improved standards of education and cancer care.

You are also a mentor for the ESTRO Fellows and for the young task force (YTF). What are your responsibilities for this role?
My role is to make available any knowledge I have of the Society, especially with regard to educational opportunities, to the younger ESTRO members. I can also act as a liaison person between young members and the ESTRO Board or Education Committee and help with the preparation of any reports the YTF has to make. However, this is a very new role for me and I think we still have to see how I can best help in response to the needs of the YTF. I am very open to any suggestions or requests.

What do you like about this role?
The chance to work with future generation ESTRO leaders and to share the knowledge I have from my years working in this field.
ESTRO FELLOW

WHAT
ESTRO Fellows are recognized by the Society as being distinguished in their competency in radiation oncology and being dedicated to their profession and to ESTRO.

WHEN
The Fellow Programme was launched in 2011 at the 30th ESTRO Anniversary Forum in London.

WHY
ESTRO wants to involve as many members as possible in Society activities so that they can learn about ESTRO’s philosophy and policy and can eventually assume increasing responsibility for Society activities. The ESTRO Fellow programme is intended to facilitate this process by identifying suitably qualified and motivated members.

WHO
At present the Fellow programme is only available for radiation oncologists, but procedures are underway to enlarge this programme to include physicists and radiation therapists (RTTs) as soon as possible.

BENEFITS
ESTRO Fellows are recognised by the Society as having both professional competence and a commitment to the Society. They are therefore identified as potential candidates for involvement in Society affairs and committees. Active participation in the Society creates many career opportunities and raises the profile of the individual, as well as giving them personal satisfaction that they are contributing towards improved standards of education and cancer care.

CRITERIA
Candidates must be board-certified specialists in radiation or clinical oncology, with at least two years post training experience.

Candidates must also have at least 50 ESTRO credits accumulated over the past five years. Credits are acquired through a range of professional activities such as attendance at ESTRO conferences (one credit per day) and courses (two credits per day), oral presentations at meetings (four credits) and publications in Radiotherapy & Oncology, the Green Journal (6 credits). Note: up to 15 such credits may be obtained through national activities related to radiation/clinical oncology.

NEXT STEPS
Candidates fulfilling these criteria can complete the application form and provide a copy of their logbook and curriculum vitae (resumé), or complete a detailed ESTRO questionnaire.

FELLOW EXAMINATION
Eligible candidates can then sit the ESTRO Fellow examination. The examination will comprise a multiple choice question paper lasting 120 minutes with each question having just one correct answer. Questions will cover all aspects of radiation oncology. To help candidates prepare for the examination a database of reference documents will be available from the ESTRO School.

Note: To make this process easier in the future, a task group is being set up to develop an interactive Fellow application form for the website. Here people could fill in the meetings and courses they have attended, the papers and abstracts accepted and the talks given at meetings, etc. The number of points accrued would automatically appear with a bar to show how far they are towards the goal of meeting entry requirements.
**ESTRO SCHOOL OF RADIOTherapy AND ONCOlogy**

**WWW.ESTRO.ORG**

<table>
<thead>
<tr>
<th>Course Title</th>
<th>Dates</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>COMPREHENSIVE QUALITY MANAGEMENT IN RADIOTHERAPY: QUALITY ASSESSMENT AND IMPROVEMENT</td>
<td>1 - 4 February 2015</td>
<td>Turin, Italy</td>
</tr>
<tr>
<td>ESTRO/EANM COURSE ON MOLECULAR IMAGING AND RADIATION ONCOLOGY</td>
<td>22 - 25 February 2015</td>
<td>Madrid, Spain</td>
</tr>
<tr>
<td>BASIC CLINICAL RADIOBIOLOGY</td>
<td>7 - 11 March 2015</td>
<td>Brussels, Belgium</td>
</tr>
<tr>
<td>PARTICLE THERAPY</td>
<td>8 - 12 March 2015</td>
<td>Paris, France</td>
</tr>
<tr>
<td>TARGET VOLUME DETERMINATION: FROM IMAGING TO MARGINS</td>
<td>13 - 16 March 2015</td>
<td>Amman, Jordan</td>
</tr>
<tr>
<td>MODERN BRACHYTHERAPY TECHNIQUES</td>
<td>15 - 18 March 2015</td>
<td>Limassol, Cyprus</td>
</tr>
<tr>
<td>DOSE MODELLING AND VERIFICATION FOR EXTERNAL BEAM RADIOTHERAPY</td>
<td>15 - 19 March 2015</td>
<td>Barcelona, Spain</td>
</tr>
<tr>
<td>3rd ESTRO FORUM PRE-MEETING COURSES</td>
<td>24 April 2015</td>
<td>Barcelona, Spain</td>
</tr>
<tr>
<td>IMAGE-GUIDED RADIOTHERAPY IN CLINICAL PRACTICE</td>
<td>10 - 14 May 2015</td>
<td>Prague, Czech Republic</td>
</tr>
<tr>
<td>CANCER SURVIVORSHIP</td>
<td>14 - 16 May 2015</td>
<td>Brussels, Belgium</td>
</tr>
<tr>
<td>ADVANCED TREATMENT PLANNING</td>
<td>16 - 19 May 2015</td>
<td>Manila, The Philippines</td>
</tr>
<tr>
<td>BIOLOGICAL BASIS OF PERSONALISED RADIATION ONCOLOGY</td>
<td>22 - 24 May 2015</td>
<td>Seoul, South Korea</td>
</tr>
<tr>
<td>MULTIDISCIPLINARY MANAGEMENT OF BREAST CANCER</td>
<td>8 - 11 June 2015</td>
<td>Florence, Italy</td>
</tr>
<tr>
<td>MULTIDISCIPLINARY MANAGEMENT OF HEAD AND NECK ONCOLOGY</td>
<td>14 - 17 June 2015</td>
<td>Beijing, China</td>
</tr>
<tr>
<td>PHYSICS FOR MODERN RADIOTHERAPY A JOINT COURSE FOR CLINICIANS AND PHYSICISTS</td>
<td>14 - 18 June 2015</td>
<td>Ljubljana, Slovenia</td>
</tr>
<tr>
<td>EVIDENCE BASED RADIATION ONCOLOGY A CLINICAL REFRESHER COURSE WITH A METHODOLOGICAL BASIS</td>
<td>21 - 26 June 2015</td>
<td>Moscow, Russia</td>
</tr>
<tr>
<td>BRACHYTHERAPY FOR PROSTATE CANCER</td>
<td>28 - 30 June 2015</td>
<td>Vienna, Austria</td>
</tr>
<tr>
<td>ADVANCED SKILLS IN MODERN RADIOTHERAPY</td>
<td>28 June - 2 July 2015</td>
<td>Copenhagen, Denmark</td>
</tr>
<tr>
<td>CANCER SURVIVORSHIP</td>
<td>14 - 16 May 2015</td>
<td>Brussels, Belgium</td>
</tr>
<tr>
<td>ADVANCED TREATMENT PLANNING</td>
<td>16 - 19 May 2015</td>
<td>Manila, The Philippines</td>
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<td>22 - 24 May 2015</td>
<td>Seoul, South Korea</td>
</tr>
<tr>
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<td>8 - 11 June 2015</td>
<td>Florence, Italy</td>
</tr>
<tr>
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<td>14 - 17 June 2015</td>
<td>Beijing, China</td>
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<td>Ljubljana, Slovenia</td>
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<td>21 - 26 June 2015</td>
<td>Moscow, Russia</td>
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<td>28 - 30 June 2015</td>
<td>Vienna, Austria</td>
</tr>
<tr>
<td>ADVANCED SKILLS IN MODERN RADIOTHERAPY</td>
<td>28 June - 2 July 2015</td>
<td>Copenhagen, Denmark</td>
</tr>
<tr>
<td>CLINICAL PRACTICE AND IMPLEMENTATION OF IMAGE-GUIDED STEREOTACTIC BODY RADIOTHERAPY</td>
<td>30 August - 3 September 2015</td>
<td>Dublin, Ireland</td>
</tr>
<tr>
<td>HAEMATOLOGICAL MALIGNANCIES</td>
<td>3 - 5 September 2015</td>
<td>London, United Kindgom</td>
</tr>
<tr>
<td>RESEARCH MASTERCLASS IN RADIOTHERAPY PHYSICS</td>
<td>3 - 6 September 2015</td>
<td>Prague, Czech Republic</td>
</tr>
<tr>
<td>IMAGING FOR PHYSICISTS</td>
<td>13 - 17 September 2015</td>
<td>Leiden, The Netherlands</td>
</tr>
<tr>
<td>BASIC TREATMENT PLANNING</td>
<td>13 - 17 September 2015</td>
<td>Lisbon, Portugal</td>
</tr>
<tr>
<td>ADVANCED TREATMENT PLANNING</td>
<td>18 - 22 September 2015</td>
<td>Lisbon, Portugal</td>
</tr>
<tr>
<td>MULTIDISCIPLINARY MANAGEMENT OF BRAIN TUMOURS</td>
<td>4 - 6 October 2015</td>
<td>Turin, Italy</td>
</tr>
<tr>
<td>IMRT AND OTHER CONFORMAL TECHNIQUES IN PRACTICE</td>
<td>4 - 8 October 2015</td>
<td>Brussels, Belgium</td>
</tr>
<tr>
<td>TARGET VOLUME DETERMINATION - FROM IMAGING TO MARGINS</td>
<td>4 - 8 October 2015</td>
<td>Budapest, Hungary</td>
</tr>
<tr>
<td>MULTIDISCIPLINARY MANAGEMENT OF LUNG CANCER</td>
<td>15 - 17 October 2015</td>
<td>Athens, Greece</td>
</tr>
<tr>
<td>ESTRO/ESOR MULTIDISCIPLINARY APPROACH OF CANCER IMAGING</td>
<td>15 - 17 October 2015</td>
<td>Brussels, Belgium</td>
</tr>
<tr>
<td>BEST PRACTICE IN RADIATION ONCOLOGY A FOUR PHASE PROJECT TO TRAIN RTT TRAINERS IN COLLABORATION WITH THE IAEA</td>
<td>19 - 21 October 2015</td>
<td>Vienna, Austria</td>
</tr>
<tr>
<td>IMAGE-GUIDED RADIOTHERAPY AND CHEMOTHERAPY IN GYNAECOLOGICAL CANCER: FOCUS ON ADAPTIVE BRACHYTHERAPY</td>
<td>1 - 5 November 2015</td>
<td>Utrecht, The Netherlands</td>
</tr>
<tr>
<td>COMBINED DRUG-RADIATION TREATMENT: BIOLOGICAL BASIS, CURRENT APPLICATIONS AND PERSPECTIVES</td>
<td>15 - 18 November 2015</td>
<td>Vienna, Austria</td>
</tr>
<tr>
<td>PAEDIATRIC RADIATION ONCOLOGY</td>
<td>19 - 21 November 2015</td>
<td>Izmir, Turkey</td>
</tr>
<tr>
<td>BASIC CLINICAL RADIOBIOLOGY ENDORSED BY ESTRO</td>
<td>21 - 24 November 2015</td>
<td>Brisbane, Australia</td>
</tr>
<tr>
<td>QUANTITATIVE METHODS IN RADIATION ONCOLOGY: MODELS, TRIALS AND CLINICAL OUTCOMES</td>
<td>6 - 9 December 2015</td>
<td>Brussels, Belgium</td>
</tr>
<tr>
<td>ADVANCED TECHNOLOGIES</td>
<td>6 - 10 December 2015</td>
<td>India</td>
</tr>
</tbody>
</table>
14TH ESO-ESMO MASTERCLASS IN
CLINICAL ONCOLOGY

7-12 March 2015
Ermatingen (Lake Constance)
Switzerland

Chairs: N. Pavlidis, GR - R.A. Stahel, CH
Scientific Co-ordinators: W. Gatzemeier, IT - R. Popescu, CH

ATTENDANCE TO THE MASTERCLASS IS BY APPLICATION ONLY
SUCCESSFUL APPLICANTS ARE GRANTED FREE REGISTRATION AND ACCOMMODATION

APPLICATION DEADLINE: 1 DECEMBER 2014
Welcome to this new issue of the Young Corner

We will start with a report on the use of mobile apps and social networks by young radiation oncologists in France. We thought that it could be an interesting topic for our readers, specially as we know that ESTRO is developing an app for the 3rd ESTRO Forum to take place in April next year in Barcelona.

As you may already know, the ECCO-AACR-EORTC-ESMO Flims workshop took place on the 21 - 27 June 2014, and three participants supported by ESTRO describe their experiences. The Flims workshop is a great opportunity for young people involved in cancer care to learn how to set up a clinical trial from start to finish.

We continue with our introduction of the members of the young task force (YTF) with interviews with Daniela Thorwarth and Pierre Blanchard.

We also have a mobility grant report from a radiation oncologist and a medical physicist from Milan, Italy who visited Aarhus University Hospital in Denmark to learn about the implementation of MRI-based adaptive brachytherapy for cancer of the cervix.

We hope you enjoy reading this issue of the Young Corner.

*Catharine Clark and Jean-Emmanuel Bibault*
Since 2009, the SFjRO (Société Française des Jeunes Radiothérapeutes Oncologues) have made apps available to calculate biological equivalent doses (eLQ) [1-3] and how to contour CT-Scans (Siriaé) [4,5] on Apple’s App Store and Google’s Play Store. These apps have since been downloaded more than 17,000 times around the world and we wanted to know how these kind of apps were actually used by young physicians.

In 2013, we performed an online survey [6], among 131 members of a summer educational session for radiation oncologists organised by SFjRO. Ninety three percent of the residents owned a smartphone and 32.8% owned a tablet. The smartphone users were more likely to use their device at work than the tablet users: 78.6% of the residents who owned a smartphone used it at work, while just 29.4% of tablet owners did so.

More than half of the residents (57%) used their smartphone more than five times a day. Most smartphone owners (91%) had at least one medical app on their phone, and 33% had more than 7 apps.
INTRODUCTION

Workshop on Methods in Clinical Cancer Research

ESTRO Young Task Force Mobility Report

Medical Apps and Social Networks

Five. Seventy eight percent of the residents used their smartphone to take pictures of lesions for diagnosis, follow-up, or to gain a second opinion. Only 30% used their smartphone to search and read articles. Overall, 68% of the residents used their smartphone to calculate equivalent doses for radiation treatments. Even if these applications had been created for academic purposes only, 67.2% of the residents used them for medical purposes which had a direct consequence on patients’ treatment, thereby breaching the apps End-User License Agreement.

It was a concern that only 60% of the residents had verified the validity of the apps they used, which could represent some risk to the patients’ treatment.

We also asked residents how they used social networks. The data showed that they were much more likely to be on Facebook than Twitter. However, only 11.2% (n=12) of them had been contacted by one of their patients through Facebook. Among these, the majority (64.3%; n=9) did not answer and simply ignored the message; 14.3% (n=2) did not answer and subsequently changed their name; and 21.4% (n=3) answered their patient via Facebook.

Seventeen percent had signed up for a dedicated physician social network, which they used to discuss anonymous patients cases, to get a second opinion, and to find help.

Young physicians in France are using their apps and social networks more and more in their work. This could have great benefits in allowing them flexibility and communication in their work, however, it is advised that any calculation apps should be validated before use.

INTERESTED IN APPS AND SOCIAL MEDIA?

• Young & ESTRO Facebook page: https://www.facebook.com/youngestro?fref=ts

• ESTRO Facebook page: https://www.facebook.com/pages/ESTRO/188685969226?fref=ts

• Twitter: @ESTRO_RT https://twitter.com/ESTRO_RT

• App at the 3rd ESTRO Forum

REFERENCES


I thoroughly enjoyed my time at the Flims workshop in June 2014. It was a fantastic opportunity to learn about the essentials of good clinical trial design, and to develop my trial protocol with the guidance of some of the world’s leading medical, radiation, surgical and paediatric oncologists and biostatisticians. The balance of the workshop was just right, with well delivered lectures each morning covering every aspect of clinical trial design and implementation, followed by protocol development group sessions and then “Small discussion groups” and “Meet-the-expert’ sessions so that you could really tailor your Flims experience to your specific needs. The protocol development group sessions were informal and relaxed, and I really enjoyed getting to know my fellow young researchers. The discussions we had made me think about my trial from angles I had not appreciated before, and change aspects of it for the better. Despite the hard work involved, it was a hugely stimulating week with a definite atmosphere of camaraderie and I felt privileged to be working alongside so many talented, creative people. I look forward to proudly sitting in the audience when they will present the results of their trials at conferences in the future and remembering that I was there when they were developed.

The whole week was set at the most beautiful backdrop of Flims, where the staff made sure we were really well looked after. The organisation of the week, the IT facilities and support were excellent and I can honestly say I had great fun. It seems like a mammoth task to write a protocol in a week, but due to the focused approach the workshop makes you take, and the support you receive, it becomes possible. It has been a unique experience where I made many new friends and colleagues from around the world, and I have come back from the workshop re-energised in my dedication to clinical research.
This spring I was honoured to attend the EC-CCO-AACR-EORTC-ESMO Workshop on Methods in Clinical Cancer Research. Within the magnificent surroundings of the Swiss mountains we had an opportunity to complete a full study protocol, which was then ready to submit to an ethics committee. The workshop provided the perfect setting for this: it created a high pressure, but very positive and productive environment, where completing a quality protocol was possible.

We attended lectures and received guidance from world class experts in the field of cancer research. There were daily sessions in small discussion groups with both the faculty and fellows, where we could brainstorm and discuss our study protocols. There were also several “Meet-the-expert” sessions, during which an appointment with any member of the faculty was feasible.

The main thing that made the workshop so remarkable to me was the ambience. Flims truly creates a very open atmosphere where any question is considered valid. All topics were open for discussion, at any time, day or night.

I would like to thank ESTRO for its support to this excellent workshop on protocol development for clinical trials. I was very lucky to participate and benefit from the 16th year of the Flims workshop with brilliant colleagues and professors from all over the world. During the workshop we had a unique chance to work not only with the faculty from our own protocol development group but also the other faculty members attending. I could not imagine any other environment where we could work so intensely and satisfactorily with mentoring from the many experts present at the workshop.
Focus on the ESTRO Young Task Force (YTF)

Initiated in 2011, the Young Task Force (YTF) is appointed by the ESTRO Board and is involved at governance level. Their mission is to support ESTRO in the development of actions for the benefit of their young colleagues from the radiation oncology area. In each issue, we introduce some of the YTF members so that you get to know your representatives within ESTRO better.

Interview with Daniela Thorwarth
Member of the YTF

Interview with Pierre Blanchard
Member of the YTF
Tell us about your training and your current employment.
In 2007, I obtained my PhD in Medical Physics from Eberhard Karls University Tübingen, Germany. During my postdoctoral research fellowship at the University Hospital for Radiation Oncology in Tübingen, I started in parallel my postgraduate training to become a certified medical physicist. Currently I am working as a research group leader in the Biomedical Physics section at the University of Tübingen.

What is your main area of interest?
I am particularly interested in the integration of functional imaging into radiotherapy planning in order to facilitate biologically individualised radiotherapy treatment in the coming years.

What does your involvement with ESTRO and the young task force (YTF) mean to you?
I joined ESTRO in 2003 and got involved with the YTF of ESTRO because I think it is very important to have a strong link with the young members of the Society. I hope the YTF can be the link that brings the young researchers of our field closer to the centre of this Society. Senior members can benefit from a close relationship with the young members in terms of enthusiasm and ideas. On the other hand, they can teach the young scientists a lot when it comes to planning a scientific career.

How do you balance research and clinical work?
I have a dedicated research position. Nevertheless, I stay in close contact with the clinical medical physicists in our department and try to be involved in some clinical tasks.

What advice would you have for new young members entering the world of radiation oncology?
Do not hesitate to ask questions, be curious, and try to get involved in areas that interest you.
Tell us about your training and your current employment.
I was trained in Paris Hospitals as a radiation oncologist and have recently completed my PhD in biostatistics/methodology. I am currently a radiation oncologist at the Institut Gustave Roussy in France. I take care of external beam radiotherapy and brachytherapy.

What is your main area of interest?
Head and neck and genitourinary cancers. I am happy to deal with these two fields of radiotherapy as they both offer a variety of clinical and technical challenges, as well as a potential for research.

When did you join ESTRO?
I joined ESTRO as a resident, and became an active member under the presidency of Professor Jean Bourhis. I have been part of the YTF since its creation in year 2011.

What does your involvement with ESTRO and the young task force (YTF) mean to you?
ESTRO is a major society, and its role in the improvement of education and career opportunities for young practitioners is important. Through the YTF, we aim to promote excellence, good practice, higher level education, and help identify and support young professionals willing to play a role in the development of the Society and the field of radiation oncology. The first YTF has achieved a strong partnership with the ESTRO Board and it is now clear that ESTRO does and will do whatever it can to support the needs of young professionals. It is fundamental that young ESTRO members who want to be involved or who have professional requests contact the YTF to fuel new propositions.

How do you balance research and clinical work?
As a young radiation oncologist, I am eager to do as much as possible, so sometimes this clinical/research ratio is not balanced. Usually my weeks consist of 75% clinical work, 10% teaching and 15% research (although I should have more time for research). It is of major importance for me
to spare free time, for family, friends and activities outside work. This allows me to be efficient and happy at work and not be overwhelmed by daily practice. I intend to do a research fellowship abroad in the coming two years.

**What advice would you have for new young members entering the world of radiation oncology?**

Try and see as much as you can. Practices vary greatly from place to place and we always learn from others. Try and be open, to physics, biology and statistics. Try to go to meetings, and attend the sessions that are outside your field of expertise. Try to exert a critical judgement regarding technical advances, and support the prospective and rigorous evaluation of those new technologies. Get involved with ESTRO.

**THE ESTRO JOB FAIR AT THE 3RD ESTRO FORUM**

25 - 26 April 2015 Barcelona, Spain

The job fair at the 3rd ESTRO Forum is certainly an opportunity not to be missed by our young colleagues.

The job fair offers a unique possibility to meet people from leading European institutions, offering jobs for young talents in the field of clinical radiation oncology, medical physics, radiation biology as well as radiation therapists. Do not miss this opportunity to discuss your plans for your personal future in radiation oncology with people from research and clinical departments during this event!

*Daniela Thorwarth, on behalf of the Young Task Force*

Read the full details on the ESTRO job fair as well as an interview with Alessandro Cortese, ESTRO CEO, in the Conference Corner on p140 >
AIM
The primary objective of our visit was to familiarise ourselves with the MRI-based treatment planning procedure adopted for cancer of the cervix brachytherapy, in particular, with respect to the combined interstitial-intracavitary technique, in order to implement this treatment modality as a standard choice at our institution.

DETAILS
Recommendations by the Gynaecological (GYN) GEC-ESTRO Working Group are exhaustive, however it was very important for us to have a practical insight into the clinical workflow of one leading European Institution - the Department of Oncology at Aarhus University Hospital.

In particular, we had the opportunity to get to the core of following issues:
• Multidisciplinary case discussions between gynaecologists, radiation oncologists and pathologists
• MRI sequences and imaging protocols for patient preparation and image acquisition, both for “pre-radiotherapy MRI examination” and “brachytherapy MRI examination”
• Pre-planning of combined interstitial-intracavitary cervix and vaginal applications of MRI-images
• Preparation in the operating theatre of combined interstitial-intracavitary gynaecological applications and hands-on experience of live cases of the clinical procedure; laparoscopic guided MUPIT (Martinez Universal Perineal Interstitial Template) implant for a vaginal recurrence of endometrial cancer
• MRI-based adaptive target contouring using imaging and clinical examination information (i.e., delineation of the GTV and definition of HR-CTV and IR-CTV); MRI-based organs at risk contouring (i.e. rectum, bladder and sigma)
• Accurate applicator reconstruction, direct and inverse treatment planning and dose distribution optimisation
• Accurate evaluation and report of the dose to targets and organs at risk.
RESULTS
Since our visit to Aarhus, we have started to implement the MRI-based treatment planning procedure as the standard choice of treatment for cancer of the cervix brachytherapy at our institution. The visit provided us with an opportunity to meet outstanding people, both from a professional and human point of view, and we really appreciated their helpfulness and their willingness to share with us their time, knowledge and daily activity.

_Cerrotta Annamaria, MD_
Radiation oncologist

_Carrara Mauro, PhD_
Medical Physicist

_Fondazione IRCCS_
_Istituto Nazionale dei Tumori_
_Milan, Italy_

Pre-implant patient examination in the operating theatre

Combined interstitial-intracavitary application in the operating theatre

Treatment plan discussion of a combined interstitial-intracavitary application
INTRODUCTION

SHOULD WE CONTINUOUSLY UPDATE THE EVIDENCE?

HEALTH ECONOMICS
INTRODUCTION

“Decision making in high technology areas for the allocation of healthcare resources is very challenging since adequate data are often lacking”

After starting four years ago, the Health Economics in Radiation Oncology (HERO) project, initiated by ESTRO, has recently completed its first work package. Three papers describing the progress made on the HERO project have just been published in the October issue of the Green Journal. In the Society Life Corner, the leaders of the project, Yolande Lievens, Cai Grau and Peter Dunscombe, comment on why HERO, and more importantly these first results, are essential for the future practice and development of radiotherapy in Europe.

Read the report on HERO in the Society Life Corner on p8 >
Economic evaluation is an accepted method for the appraisal of health care programmes and is increasingly used to make informed decisions about the efficient allocation of healthcare resources. To date, economic evaluation has been mainly applied to pharmaceutical interventions. Less attention has been paid to other types of intervention, including those involving advanced health technologies in radiotherapy. Decision making in high technology areas is much more challenging since adequate data are often lacking. Recently Barbieri and colleagues [1] performed a systematic review of published cost-effectiveness studies of radiotherapy for breast, cervical, colorectal, head and neck and prostate cancer. They compared the economic evaluation methods applied in these published studies with those defined in the guidelines used by the National Institute for Health and Care Excellence (NICE) technology appraisal programme.

The elements of an economic evaluation that are generally recommended as best practice for undertaking a high-quality study were considered as essential requirements, and included the following seven:

1. Comparators clearly defined and justified
2. Patient group/indication clearly described
3. Effectiveness evidence based on a systematic review
4. Data for measurement of health-related quality of life (HRQoL) reported directly by patients and/or carers
5. Appropriate time horizon
6. Relevant one-way sensitivity analyses
7. Probabilistic sensitivity analysis (PSA) used to quantify full uncertainty.

A systematic review of five tumour types was undertaken and a total of 3,358 titles and abstracts were initially identified (794 for breast, 623 for colorectal, 707 for prostate, 325 for cervical, 909 for head and neck). After excluding duplicates and studies that clearly did not meet predefined inclusion criteria, 116 full papers were retrieved (18 each for breast and colorectal, 37 for prostate, 13 for cervical, 30 for head and neck) for more detailed study. Of these, 29 generally satisfied the inclusion criteria and were included in the final review (14 for breast, two for colorectal, ten for prostate, none for cervical, three for head and neck).

Among the seven criteria that were defined as essential requirements, four were met in the majority of studies and these were: comparators clearly defined, patient group/indication clearly defined, appropriate time horizon and relevant one-way sensitivity analyses. In 27 (93%) of the studies, the interventions/comparators of the analysis were clearly defined and two prostate cancer studies did not have a clear description of the interventions compared. Quality-adjusted life-years (QALYs) were used as the main outcome measure in 26 of the 29 studies (90%). The inclusion of HRQoL preference data assessed by a representative sample of the public was rare, with only three of 26 (10%) analyses using these general measures.
population weights. In most cases (14 of 26, 54%), little detail on the sources of the valuation of HRQoL data was provided and it is unclear whether or not these were taken from the general public.

One of the main findings was that there was substantial heterogeneity in the used methods. Overall, three key elements considered essential for a good-quality evaluation (effectiveness evidence based on a systematic review, data for measurement of HRQoL reported directly by patients and/or carers, use of PSA to quantify the uncertainty) were generally not fulfilled in the 29 included studies.

A strength of NICE is the provision of an explicit cost-effectiveness threshold to judge the value for money of the intervention considered. However not explicitly defined in the NICE reference case but of considerable importance, is the impact of heterogeneity in the cost effectiveness of treatments across different subgroups of patients. In the case of cancer, the identification of specific types of patients for whom radiotherapy is cost effective appears to be a key issue. For example, in the case of breast cancer, an ongoing meta-analysis by the Early Breast Cancer Trialists’ Collaborative Group (EBCTCG) of over 10,000 women treated in clinical trials with and without radiotherapy, has shown that, overall, breast radiotherapy reduces any cancer recurrence by 50%. However, although the relative advantage of breast radiotherapy is constant, the absolute benefit for individuals varies depending on their risk of recurrence and this, in turn, drives the cost effectiveness of radiotherapy in these patients. It is likely that, in a very low-risk group of patients, radiotherapy would not be cost effective. The same can be stated of prostate cancer, in which the relative merits of radiotherapy versus watchful waiting for low-risk disease has not been tested but is unlikely to demonstrate improvements in disease-specific survival up to 10 years of follow-up, since a comparison of radical prostatectomy and watchful waiting has shown no survival benefit.

The authors concluded that there is a dearth of up-to-date, robust evidence on the effectiveness and cost effectiveness of radiotherapy in cancer. The number of published economic evaluations of radiotherapy using QALYs or life years gained (LYs) appears quite low. For example, only two studies were found for colorectal cancer, three for head and neck cancer and none for cervical cancer. Some essential methodological standards were generally not met, especially in the identification of the clinical evidence. Radiotherapy techniques used in the cancer areas investigated have evolved rapidly over the last decade and many newer techniques are currently being evaluated in clinical trials. In addition, the clinical evidence in many of the studies is old and a number of new trials describing novel radiotherapy interventions have been reported, or are currently ongoing. Consequently, the full uncertainty associated with the clinical benefits of the interventions was rarely captured. As new, relevant evidence becomes available, additional cost-effectiveness evaluations should be undertaken to inform decision makers regarding current and future clinical practice in radiotherapy.

Madelon Pijls
MAASTRO
Health insurance company CZ,
Tilburg, The Netherlands

REFERENCE
PROJECTS & RESEARCH
With the number of ion therapy treatment centres in Europe increasing, there is a growing need for a network of research facilities for the development of appropriate instruments for high-performance ion therapy. The Union of Light Ion Centres in Europe (ULICE) project was launched in 2009 to address this need to provide more particle therapy research facilities and encourage collaboration among existing and planned centres within the ion therapy community.

ULICE is an infrastructure project which was funded by the European Commission for four years, under the umbrella of the European Network for Light Ion Therapy (ENLIGHT) and coordinated by the Italian centre for hadrontherapy CNAO. The ULICE project consists of three pillars: Networking Activities (NA), Joint Research Activities (JRA) and Transnational Access (TNA). The project was extended by one year to allow the deliverables to be met and the closing meeting was held on 12 July 2014 at CERN, the European Centre for Nuclear Research.

**NETWORKING ACTIVITIES (NA) PILLAR**
During the ULICE project the NA pillar was responsible for internal communications amongst the 175 members of the consortium, and external activities reporting the project’s activities to the world. There have been a number of flyers, news articles in the ENLIGHT HIGHLIGHTS, presentations at international conferences and a video which was produced to help promote the beam time available in TNA. More recently an...
animation has been created to simulate a virtual ion therapy centre with an interactive map communicating major aspects within an ion therapy facility. The animation can be found here: www.cern.ch/virtual-hadron-therapy-centre

In 2009, a Training and Education Committee (TEC) was set up to provide travel grants to attend courses and/or workshops and to facilitate exchange visits.

Some of the courses included:
- Radiotherapy with protons and ions which was held at the National Italian Center for Oncologic Hadrontherapy (CNAO) in Pavia, Italy, in March 2013. Of 58 participants, four were junior scientists from the consortium supported by ULICE grants
- Clinical practice and implementation of image guided stereotactic body radiotherapy which was held in Wurzburg, Germany in September 2012.

The NA pillar was also responsible for organising five annual workshops at different locations around Europe which were attended by over 100 participants each year, bringing together the ULICE consortium with other members of the ENLIGHT community.

TRANSNATIONAL ACCESS (TNA) PILLAR
The TNA pillar was responsible for providing beam time for patient treatment with particle therapy, as well as research projects committed to improving particle therapy. There were two access providers, the National Italian Center for Oncologic Hadrontherapy (CNAO) in Pavia and the Heidelberg Ion-Beam Therapy Centre (HIT) in Germany. During the last phase of the project, the budgeted number of hours was mainly used for preclinical research projects.

Beam time was promoted in several ways, through a video which showed the main scientific events related to the ion therapy world, publications, announcements on the project website and communications to the IAEA (International Atomic Energy Agency) and others. As the beam time had to be also provided internally to the consortium for research activities, the coordinator informed the beneficiaries of the availability of beam time with several messages.
Ten applications were received and these were evaluated by a selection panel of external and internal members of CNAO and HIT, in order to guarantee transparency during the procedure. In 2012, the facility in Heidelberg began the TNA activities providing beam time to two groups of researchers who had been working on detectors for radiation. In the last phase of the project, at CNAO, many research groups visited from January to August to use beam time. Their main goals were to test the instruments they were developing, to gather hands-on experience in radiation measurements, and to develop long-lasting networks with experts in radiation detection around the world. The research groups consisted of young researchers of seven nationalities brought together by ULICE, a single funded EU project. Both proton and carbon ion beams were used for more than 35 hours.

Regarding clinical access, it is worth noting that CNAO only recently received authorisation for the clinical use of the synchrotron and consequently the clinical routine procedure was only initiated at the beginning of 2014. The Italian centre also had the possibility to test the referral of patients from outside Italy through some foreign patients coming from France and the UK.

**JOINT RESEARCH ACTIVITIES (JRA) PILLAR**
Because of the recognition of a large need for research mandatory for promoting the field of light ions with regard to therapeutic applications, a significant space within ULICE was attributed to the development of research infrastructure and to promote specific research activities. Therefore, six work packages (WPs) were designed to meet these challenges, and they addressed the following topics:

**Ion therapy for intra-fractional moving targets (WP4)**
- 4D imaging, deformable image registration, and motion modelling with a precision that is sufficient for particle therapy treatment planning and delivery
- Motion monitoring system that can provide precise target position information on a timescale of milliseconds
- Tracking system prototype for CNAO
- Rescanning functionality at UKL-HD
- Workflow concepts including radiation protection aspects for 4D ion radiotherapy.

**Adaptive treatment planning for ion radiotherapy (WP5)**
- Variation of radiosensitivity
- Mixed beam treatment
- Time dose fractionation
- Variation of anatomy/topography.

**Carbon ion gantry (WP6)**
- Functional specification
- Conceptual design.

**Common database and grid infrastructures for improving and catalysing access to RI for the broad European community (WP7)**
- Framework of IT services to support data sharing and semantic inter-operability across the entire project, and with existing cancer grids, enabling the project to achieve maximum impact in the shortest possible time, and at minimum cost
- Services for case referral, scheduling and treatment management – using architectures that facilitate privacy, anonymity and security – in support of all other work-packages
- Support for development of common multilingual vocabularies, data items, protocols, workflows to facilitate data sharing across the entire European ion therapy grid and to facilitate health economics statistics
- Improvement of future European decision making, operational efficiency, quality assurance, data analysis, publication of results and teaching opportunities in this area.

The detailed work performed within these work packages can be assessed through the deliverables (n=53) which are available at the ULICE homepage: http://ulice.web.cern.ch/ULICE/cms/index.php?file=home.

The two remaining work packages on research infrastructure (WP2) and on biologically based expert system for individualised patient allocation (WP3) will be covered in more detail in the next issue of the ESTRO newsletter.

Roberto Orecchia, Project coordinator
Manjit Dosanjh, Networking Activities (NA)
Jürgen Debus, Transnational Access (TNA)
Richard Pötter, Joint Research Activities (JRA)

On behalf of the ULICE Consortium
ULICE project: Contract N° 228436 was EU funded under FP7 Capacities Research Infrastructure
INSTITUTIONAL MEMBERSHIP
INSTITUTIONAL ESTRO MEMBERSHIP

The Institutional Membership category has been especially designed for European hospitals, clinics or other institutions that seek to continuously develop and support their radiotherapy and oncology professionals. In this Corner we invite our institutional members to provide us all with some feedback on their experience and institute.

In this issue we highlight the UPMC San Pietro FBF in Rome, Italy with Professor PierCarlo Gentile.
How would you describe the radiotherapy department of your institute?
The highly specialised UPMC San Pietro FBF Radiotherapy Centre offers patients innovative treatments and advanced care protocols. Our multidisciplinary team uses the newest and most sophisticated technologies, ensuring the highest possible accuracy of radiotherapy care.

UPMC San Pietro FBF is part of the San Pietro Hospital, a 500 bed facility with a radiotherapy department offering conformational and Intensity-Modulated Radiation Therapy (IMRT) treatments through two linear accelerators. The two departments (eight physicians, six physicists, 12 therapists and six nurses) offer care to an average of 120 patients a day.

What are the main areas of specialisation in your department?
At the UPMC San Pietro FBF Advanced Radiotherapy Centre, we focus on stereotactic (SRS/SBRT) treatments, using a dedicated linear accelerator (Varian TrueBeam Stx). We also perform Rapid Arc, IMRT/Image Guided RadioTherapy (IGRT), using Exactrac system and a six degree of freedom robotic couch to improve our treatments’ accuracy.

What are the main achievements so far and the main challenges on your daily work and for the future?
With only 18 months of clinical activity, the UPMC San Pietro FBF Advanced Radiotherapy Centre can count on UPMC decennial experience in radiosurgery, and this from the first day of operational activity. This collaborative approach has enhanced UPMC San Pietro’s clinical expertise.

UPMC San Pietro FBF is part of the UPMC Cancer Centre, one of the largest cancer networks in the United States. The UPMC cancer centres’ network includes 38 facilities in the US, and one cancer centre in Ireland, providing high-standard care to more than 72,000 patients a year. The ongoing collaboration with the UPMC Cancer Centres’ network also provides for case reviews, second opinions and the development of clinical protocols to manage the treatment of cancer patients.

We are working to build a “hub and spoke” relationship with the other UPMC facilities both in the US and Italy (ISMETT in Palermo, UPMC Institute ▼)
for Health in Tuscany). We are focusing on leveraging our broad network of treatment facilities to provide access to the breadth of clinical expertise offered at our locations around the globe.

Is your department currently undertaking some studies or clinical trials that you would like to share with the ESTRO Community?
The UPMC Cancer Centres network is also affiliated with the University of Pittsburgh Cancer Institute (UPCI), one of the leading institutions for research in cancer care (more than 4,500 articles published over the last five years and more than $146 million received by the National Institute for Health in 2013). UPMC San Pietro FBF is actively involved in several of the 440 currently active clinical trials at UPCI. The centre is also working on new radiotherapy protocols for lung and prostate cancer.

In your opinion, what additional benefits would be useful as part of the institutional membership package?
It would be useful to have a website dedicated to calls for ongoing clinical trials being developed at the European level.

Is there anything particular about your institute that you would like to promote and share with the ESTRO Community?
UPMC San Pietro FBF’s physicians and therapists have been trained in Pittsburgh. In addition to their clinical expertise, UPMC provides the centre with operational policies and procedures. Its experience in operating in over 40 cancer treatment sites, allows us to rapidly improve the quality of care provided in the region while maintaining high levels of efficiency.

FACT FILE
UPMC SAN PIETRO FBF
Rome, Italy

Description of the institution
The highly specialized UPMC San Pietro FBF radiotherapy centre offers patients innovative treatments and advanced care protocols.

Areas of specialisation
At the UPMC San Pietro FBF advanced radiotherapy centre, we focus on stereotactic (SRS/SBRT) treatments. We also perform IMRT/IGRT, using Rapid Arc, ExacTrac system and a six degree of freedom robotic couch to improve our treatments’ accuracy.

Equipment used in the RO department
• Truebeam™ STx
• RapidArc®
• IMRT - Intensity Modulated Radiation Therapy
• IGRT - Image Guided RadioTherapy
• Exactrac
• 6 degree of freedom couch
• CT (TAC) 64 slide computed tomography
ESTRO CONFERENCES
Let’s be clear, entering the winter season is not the most fun time of the year. However, just picture yourself travelling to the next ESTRO conference and this might raise the temperature and heat you up.

Firstly in February 2015, we will go to Nice, France to the 5th International Conference on innovative approaches in Head and Neck Oncology (ICHNO). The three Chairpersons of this multidisciplinary meeting streamline the objectives of the conference and give us some background information on head and neck oncology in their disciplines.

Then in April 2015, we will head to Barcelona for the 3rd ESTRO Forum. In 2013, 3,000 of you joined us joined us in Geneva so we are counting on you to break the record for this event which has now become the gathering for the whole radiation oncology community. The radiation oncology community are looking forward to absorbing brilliant science in their own disciplines but also through building bridges between all the disciplines which are the strength of the Forum. Also, for the first time during the Forum ESTRO’s job fair will be held. The ESTRO CEO, Alessandro Cortese, highlights for us the added value for job seekers and employers of participating in such a concept.

*Agostino Barrasso and Eralda Azizaj*
FOCUS ON NEXT ESTRO CONGRESSES

3RD ESTRO FORUM
24 - 28 April 2015
Barcelona, Spain

5TH ICHNO
International Conference on Innovative Approaches in Head and Neck Oncology
12 - 14 February 2015
Nice, France

EUROPEAN CANCER CONGRESS
25 - 29 September 2015
Vienna, Austria
EDUCATION: WHAT NOT TO MISS

3rd ESTRO Forum
24 - 28 April 2015
Barcelona, Spain

PRE-MEETING COURSES
FRIDAY 24 APRIL 2015

- **Clinical pre-meeting course:**
  Data management
  *Course directors: Glenn Jones (Canada) and André Dekker (The Netherlands)*

  **Course aim**
  To strengthen capacity in quantitative research through a more professional handling of data in clinical research, thereby proving, improving and transforming the quality of health care.

- **Physics pre-meeting course:**
  From 4D Imaging to 4D Delivery
  *Course directors: Per Poulsen (Denmark) and Uwe Oelfke (UK)*

  **Course aim**
  The accuracy of high precision radiation therapy is often compromised by organ motion. The specific problem of intrafraction organ has been addressed through various technical developments and research on this topic within the last decade. However, effective clinical implementation of a complete 4D-workflow has still not been accomplished in the majority of radiation therapy departments. This course will give an overview of the latest developments, current status and challenges related to the clinical application of 4D radiotherapy.

- **GEC-ESTRO workshop:**
  Adaptive brachytherapy strategies
  *Course director: Jacob Lindegaard (Denmark)*

  **Course aim**
  At this point in time, adaptive brachytherapy has mainly been used in prostate and gynaecological brachytherapy. However, the potential is huge for other sites and also for further developments such as sub-volume boosting. It is the aim of this GEC-ESTRO workshop to give an overview of the current status of adaptive brachytherapy and also to explore the potential for further developments of this successful strategy.

IMPORTANT DATES
- **Abstract submission deadline:** 20 November 2014
- **Early registration deadline:** 15 December 2014
- **Late registration deadline:** 24 March 2015
- **Desk registration:** from 25 March 2015
**Intedisciplinary pre-meeting course:**
Incorporating imaging in radiation oncology treatment delivery
*Joint ESTRO-EIBIR-EANM*
*Course directors: Vincenzo Valentini (Italy), Gabriel Krestin (The Netherlands), Valerie Lewington (UK)*

Course aim
To foster understanding of imaging contribution in the delivery of tailored dose by new radiotherapy technologies and to be updated on new opportunities for imaging guided radiotherapy.

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**RTT PRE-MEETING COURSE:**
Implementing of SBRT and SRS: a review of current practice
*Course directors: Filipe Garcia Moura (Portugal) and Philipp Scherer (Austria)*

Course aim
To introduce and develop the concept of stereotactic body radiotherapy (SBRT) and stereotactic radiosurgery (SRS) in clinical practice. The course will provide participants with the theoretical background to implement SBRT and SRS in safe environments, which will enable the development of new skills and competences for advanced treatment strategies.

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**CONTOURING WORKSHOPS**
Eight contouring workshops have been planned (each session is repeated once):

- Oesophagus
- Lymphoma (joint with ILROG)
- Prostate cancer in the post-prostatectomy setting (NEW)
- Organs at risk for the upper abdomen (new)

**Target audience**
The delineation workshops are aimed at all radiation oncology professionals who want to improve their contouring skills:
- Radiation oncologists will delineate a common case, a rare case and a more advanced case
- RTTs and dosimetrist will delineate the OAR case.

Dates and times to be announced soon.

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**INTERACTIVE MULTIDISCIPLINARY TUMOUR BOARD SESSIONS**

**Saturday 25 April 2015**
10.30-11.30
Upper GI

**Sunday 26 April 2015**
10.30-11.30
Prostate

**Monday 27 April 2015**
10.30-11.30
Lung

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**USEFUL LINKS**
More information on the pre-meeting courses: [http://www.estro.org/congresses-meetings/articles/3rd-forum-education >](http://www.estro.org/congresses-meetings/articles/3rd-forum-education >)
INTERVIEW WITH ALESSANDRO CORTESE, ESTRO CEO

With thousands of delegates expected from all over the world, the 3rd ESTRO Forum represents a gathering of individuals with highly specialised profiles brought together in the same place and at the same time. ESTRO offers job seekers and employers dedicated booths space in the congress centre to hold job interviews, essential to facilitate exchanges. Alessandro Cortese, the ESTRO CEO, describes the essence of this project.

**Why is ESTRO launching a job fair?**

ESTRO is a society that has a dual dimension. It is a scientific society but it is also a professional society. The mission of ESTRO is to help radiation oncologists, medical physicists, radiation therapists, brachytherapists and radiobiologists, all the different disciplines involved in radiation oncology, to evolve professionally during the course of their career. Of course, traditional ways are linked to education, the core curricula that are published, and all sorts of activities that we do, to create a common practice and a high level practice. However, there are also needs that are specific to different stages of the career of the people involved with ESTRO. We thought that especially during the early career stages it would be interesting and make sense to create an environment to exchange the need from employers and the interest from potential candidates. We were already aware that this type of activity was happening during the congresses so we thought that we would create a dedicated platform to allow this to happen in a structured way at the ESTRO annual meeting.

**Do you mean that the job fair is more targeting the young?**

It is not limited to young individuals but I would tend to suspect that yes it will target the young, although everyone is welcome to participate. We cannot predict what will be the openings or possibilities but I’m quite sure that if there is a high level position/opening, the confidentiality that would need to apply before will still be required for some positions, with or without the job fair.
But with the structure we have put in place, this job fair will probably target mainly the starting phases of people's careers.

**Why are you launching the job fair for the first time at the 3rd ESTRO Forum?**

We are launching the job fair now because there is a growing need that has been requested by our members. We are organising it during the Forum because we believe the structure, where all the disciplines have their own meeting, allows it to happen. The participants clearly network within disciplines so it made sense that opportunities for job seekers happen around the concept of a discipline where they belong to, so that they can meet potential employers but outside of the mechanism where they usually network.

**What is the main asset of the ESTRO job fair for job seekers/delegates? What is the added value compared to the other usual employment channels?**

The added value is quite simple. There is no similar event as the job fair that is dedicated to radiation oncology. ESTRO’s annual meetings are the times of the year where you have the highest density of people involved in radiation oncology. We expect that from a job seekers point of view you will get more openings in one place than you would have any other time during the year.

**Does the sector of radiation oncology usually actively recruit?**

I think so. There are mainly two streams of employment, the academic sector and clinical practice, public or private. In that sense the academic stream is probably working in a way that is external to the job fair but there are many centres in many countries that are actively recruiting for radiation oncology disciplines. And then companies of course obviously look for people with a scientific background.

**Regarding institutes and companies, how can the ESTRO job fair represent a unique opportunity to find the ideal candidate?**

They will probably get a higher quality of recruitment potential at the ESTRO Forum meeting than they would have outside. Knowing that this is not a competitive mechanism as to what would happen with the usual channels of recruitment where people can make direct contact with employers but that there will be an opportunity for both to increase their chances either to find a good position or to determine the candidate that is the highest possible profile for the position.

Also, from a geographical aspect, the recruiting companies and centres will be able to conduct interviews during the job fair so this is convenient to have the opportunity to meet people face to face as opposed to CVs sent by email or telephone interviews.

**Are there any disciplines or profiles that will be more specifically sought by the recruiting companies and institutes?**

That is difficult to respond to without any previous experience. It will be a nice opportunity for all the disciplines. We know that the disciplines have different roles and functions so depending on the demand, we will see who will benefit the most from this initiative. I am guessing that medical physicists would probably be the ones to benefit the most from this job fair but again this is a guess and not based on any data.
THE ESTRO JOB FAIR AT THE 3RD ESTRO FORUM

WHAT?
Two days where participants at the 3rd ESTRO Forum will have the opportunity to meet the industry and institutes for job interviews in a separate area within the congress centre.

WHERE?
Interviews will be held in the job fair area, located in the registration hall. Each participating company will have a specific booth designed to welcome participants and job seekers from the radiation oncology field. In addition, all employers with a booth in the job fair will have the opportunity to rent a meeting room in the congress centre for half a day or more, in order to conduct on-the-spot interviews in a more confidential environment.

WHEN?
Saturday 25 April 2015 from 13.00-18.00 hrs
Sunday 26 April 2015 from 8.00-14.45 hrs

WHO?
Participating in the job fair are:
- Candidates: all the 3rd ESTRO Forum participants will have free access to the job fair.
- Employers: exhibiting companies at the 3rd ESTRO Forum and all the 2015 ESTRO institutional members (institutes).

HOW?
- Candidates: entrance to the job fair is free to all the 3rd ESTRO Forum participants. No pre-registration is needed.
- Employers will need to book a specific Job Fair booth:
  - Interested companies should contact Valérie Cremades, vcremades@estro.org
  - Interested institutes should contact Myriam Lybeer, mlybeer@estro.org.
5th ICHNO
International Conference on innovative approaches in HEAD & NECK ONCOLOGY
12 - 14 February 2015
Nice, France
What are the current challenges for radiation oncology in head and neck?

According to the ESTRO vision for 2020, the fantastic rate of advances in science, biology, physics and imaging will, no doubt, allow radiation therapy to be more efficient and better tolerated in head and neck cancer, with an increasing proportion of patients being tumour-free with fewer side effects.

Of particular importance to improve the outcome of radiation therapy in head and neck cancer is the generalisation of high precision radiotherapy and its combination with molecular imaging, with new molecular targeted drugs and with new immunotherapy approaches.

Record number of abstracts submitted to the 5th ICHNO: we received 153 abstracts!

This is the fifth edition of the conference. What is new this year? Are there any new aspects in the programme?

All these new developments will be tackled at the conference, which has a very unique focus on innovation and translational research in all the major fields of head and neck cancer.

Are there any sessions more specifically that you look forward to attending?

This conference is a unique one, having built its success on combining innovation but also on strongly promoting multidisciplinarity. The beauty of the meeting is related to its format, with all the presentations being given in a single room, allowing in turn interactions between surgeons, medical and radiation oncologists along with other specialists in head and neck cancer. Of special interest are the sessions on randomised trials, the debates and also the sessions mimicking a tumour board.

We really look forward to seeing and welcoming you in Nice for this 5th edition of ICHNO!
What are the recent evolutions of the treatment of head and neck cancers?
After the impressive revolution in reconstructive surgical capabilities and their refinement during the end of the last century, we have come to learn over the last decade that treatment should be individualised and that it can be different for two patients with a similar tumour site and stage. Important factors to take into consideration are the biology of the tumour, the comorbidity of the patient and also the wishes and expectations of the patient.

Examples of novel surgical treatments are the use of robotic surgery and sentinel node procedures. Both aim at minimising morbidity and maximising quality of life while maintaining safe oncological outcome, and they are increasingly applied. We are only at the beginning of this evolution and are just starting to find out which patients benefit most from these. Furthermore, developments in radiation therapeutic possibilities as well as in medical oncology go hand in hand with the surgical advancements. The optimal use of the combined use of these three modalities for the patient with advanced head and neck cancer will continue to be the challenge ahead of us.

How is the ICHNO meeting different from the EHNS meeting that took place last April in Liverpool?
Both meetings really complement each other. The biannual European Head and Neck Congresses aim at providing a leading forum for presenting the latest innovating research, both basic and clinical, in the field of head and neck oncology in Europe. The ICHNO meetings have the advantage of bringing together three major societies supplementing each other and providing the best blend of cutting-edge developments in surgery, radiation and medical oncology. Thus they provide a forum for improved multidisciplinary diagnosis and decision making as well as establishing future roads of basic research and trials.

Who should participate at the conference?
We want to attract both the young as well as the accomplished clinician working within the field of head and neck oncology, by inviting the very best European as well as overseas speakers on the diagnosis and treatment of head and neck cancer, as well as basic research in this field.
**Why is it important to have a multidisciplinary conference in head and neck oncology?**

The approach to patients with head and neck cancer is complicated and requires the contribution of different specialties. Many patients are cured but suffer the devastating consequences of treatment, such as speech and swallowing impairment. Therefore, it is important to select the most suitable treatment for the individual patient. Furthermore, most patients are not cured with a single modality as the majority are diagnosed with an advanced disease stage. A meeting where the experts of the different specialties meet and exchange information on the advances in their fields and discuss the state-of-the-art management of these challenging patients is very important.

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**What are the current challenges in medical oncology in head and neck?**

The challenge in the treatment of patients with head and neck cancer is to optimise efficacy while minimising treatment-related acute and late toxicities. We need to identify good prognosis patients and investigate whether the de-intensification of treatment affects treatment results. We know for example, that human papillomavirus-associated head and neck tumours have a better prognosis compared to tobacco-related stage-matched counterparts. De-intensification studies are ongoing in this population. On the other hand, advanced head and neck cancers in non-smokers carry a poor prognosis despite innovations in surgery, radiotherapy and chemotherapy. The latter subgroup is in great need for novel treatments.

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**Will the topic of "personalised medicine" be tackled during the conference?**

Personalised medicine is the future of cancer treatment. Our conference will focus on treatment approaches in good and poor prognosis patient subsets, novel treatment approaches as well as the classification of patients based on molecular and imaging tools.
18th ECCO - 40th ESMO
European Cancer Congress
Reinforcing multidisciplinarity
VIENNA, AUSTRIA, 25 - 29 SEPTEMBER 2015

The largest multidisciplinary platform for presenting groundbreaking data to a global audience.

REGISTER NOW

www.europeancancercongress.org
18th ECCO - 40th ESMO
EUROPEAN CANCER CONGRESS
Reinforcing Multidisciplinarity
25 - 29 September 2015
Vienna, Austria
In collaboration with ESTRO

KEY DATES

- 1 Oct 2014: Early registration opens
- 26 Jan 2015: Abstract submission opens
- 7 Apr 2015: Early rate registration deadline
- 28 Apr 2015: Abstract submission deadline
- 29 Apr 2015: Fellowship grant application deadline
- 22 Jul 2015: Late breaking abstract submission opens
- 4 Aug 2015: Regular rate registration deadline
- 5 Aug 2015: Late breaking abstract submission deadline
- 18 Sep 2015: Late rate registration deadline
- 25 - 29 Sep 2015: Congress in Vienna
INTRODUCTION

FOCUS ON NEXT ESTRO CONGRESSES

29 April - 3 May 2016
Turin, Italy
CALENDAR OF EVENTS
2014

NOVEMBER

6 - 8 November
10th Meet The Professor Advanced International Breast Cancer Course (AIBCC)
Padua, Italy
*ESTRO recommended event*
http://meettheprofessor.accmed.org/ >

13 November
ESTRO session at RUSSCO 2014
Moscow, Russia
*ESTRO endorsed event*

13 - 14 November
International symposium on HPV infection in head and neck cancer
Poznan, Poland
*ESTRO endorsed event*

14 - 16 November
EMUC 2014 - European Multidisciplinary Meeting on Urological Cancers
Lisbon, Portugal
http://www.emuc2014.org/ >

23 - 25 November
7th European Multidisciplinary Colorectal Cancer Congress (EMCCC)
Amsterdam, The Netherlands
*ESTRO endorsed event*
http://www.dccg.nl/conferences/emccc2014/word-of-welcome/ >

28 - 30 November
Interdisciplinary teaching course on head & neck brachytherapy
Rome, Italy
*ESTRO supported course*
http://www.brachiterapiaitalia.it/ENTcourse/ENT_course/Home.html >

DECEMBER

4 December
2nd GEC-ESTRO Workshop
Brussels, Belgium
http://estro.org/congresses-meetings/items/2nd-gec-estro-workshop >

5 December
GEC-ESTRO *in vivo* dosimetry seminar
Brussels, Belgium
### 2014

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| 11 - 13 December | SBRT symposium 2014  
Amsterdam, The Netherlands  
*ESTRO recommended event* |

### 2015

#### FEBRUARY

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| 12 - 14 February | 5th ICHNO  
Nice, France  
*ESTRO, ESMO and EHNS joint event* |

#### MARCH

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| 12 - 14 March | Advanced prostate cancer consensus conference 2015  
St. Gallen, Switzerland  
*ESTRO recommended event* |
| 22 - 26 March | Radiobiology & radiobiological modelling in radiotherapy course  
Port Sunlight, Wirral, UK  
*ESTRO supported course* |

[http://www.sbrt.eu/](http://www.sbrt.eu/)  
[http://www.estro.org/congresses-meetings/items/5th-ichno](http://www.estro.org/congresses-meetings/items/5th-ichno)  
**2015**

**MAY**

25 - 29 May
15th International Congress of Radiation Research (ICRR 2015)
Kyoto, Japan

*In collaboration with ESTRO*

http://www.congre.co.jp/icrr2015/ >

**JUNE**

20 - 22 June
Wolfsberg Meeting
Wolfsberg, Switzerland

*In collaboration with ESTRO*

http://www.wolfsberg-meeting.com/ >

**SEPTEMBER**

25 - 29 September
European Cancer Congress 2015 (ECC2015)
Vienna Austria


**APRIL**

27 - 28 March
Trends in Central Nervous System Malignancies
EORTC-EANO-ESMO Conference
Istanbul, Turkey

*ESTRO endorsed event*

http://www.ecco-org.eu/EEE2015 >

14 - 15 April
5th European Lung Cancer Conference (ELCC)
Geneva, Switzerland

*In collaboration with ESTRO*

Abstract submission now open (until 7 January 2015)

http://www.esmo.org/Conferences/ELCC-2015-Lung-Cancer >

24 - 28 April
3rd ESTRO Forum
Barcelona, Spain

*ESTRO interdisciplinary congress*

http://www.estro.org/congresses-meetings/items/3rd-estro-forum >
2015

NOVEMBER

12 - 15 November
EMUC
7th European Multidisciplinary Meeting on Urological Cancers
Barcelona, Spain

Joint EAU, ESTRO and ESMO conference

2016

APRIL

29 April - 04 May
ESTRO 35
Turin, Italy

ESTRO congress