

### Material and Methods

In this multicentre phase III randomised controlled trial, MPM patients following a chest wall procedure were randomised 1: 1 to receive PIT (within 42-days of procedure) or no PIT. Large thoracotomies, needle biopsy sites and indwelling pleural catheters were excluded. PIT was delivered at a dose of 21Gy in 3 fractions over 3 consecutive weekdays using a single electron field adapted to maximise coverage of the tract from skin surface to pleura. The primary outcome was the incidence of CW metastases within 6 months from randomisation, assessed in the intention-to-treat population. Stratification factors included epithelioid histology and intention to give chemotherapy. Trial registration number NCT01604005.

### Results

375 patients (186 PIT and 189 no PIT) were randomised between 06/2012-12/2015 from 54 UK centres. Comparing PIT vs no PIT, %male patients was 89.8/88.4%, median age 72.8/74.6 years, %ECOG PS (0,1,2) 32.2,56.5,11.3/23.8,56.1,20.1%, %confirmed epithelioid histology 79.6/74.1%, and %with intention to give chemotherapy 71.5/71.4%. The chest wall procedures were VATS (58.1/51.3%), open surgical biopsy (2.7/5.3%), local-anaesthetic-thoracoscopy (26.9/27.0%), chest drain (5.9/8.5%) and others (6.5/7.9%) for the PIT vs no PIT arm respectively. Radiotherapy was received as intended by 181/186 patients in the PIT arm. The proportion of CW metastases by 6 months was 6/186 (3.2%) vs 10/189 (5.3%) for the PIT vs no PIT arm respectively (odds ratio 0.60 [95% CI 0.17-1.86];  $p=0.44$ ) and by 12 months 15/186 (8.1%) versus 19/189 (10.1%) respectively (OR=0.79 [95% CI 0.36-1.69];  $p=0.59$ ). Cumulative incidence of CW metastases at 6months/12 months/24 months was 3.3/8.5/10.0% in the PIT arm vs 5.6/10.9/18.7% in the no PIT arm. Evaluable patients who developed CW metastases reported a mean increase in visual analogue scale pain score of 13.3 ( $p<0.01$ ) compared to baseline. Skin toxicity was the most common radiotherapy-related adverse event in the PIT arm with 96(51.6%) grade 1, 19(10.2%) grade 2, and 1(0.5%) grade 3 radiation dermatitis (CTCAE V4.0). There were no other grade 3 or higher radiotherapy-related adverse events.

### Conclusion

There was no significant difference in incidence CWM between the 2 groups and the increase in VAS pain score in patients with CWM was below the 20% increase which we considered clinically significant. There therefore is no role for the routine use of PIT following diagnostic or therapeutic CW procedures in patients with MPM.

### OC-0538 Daily versus weekly prostate cancer image-guided radiotherapy: A Phase 3 randomized trial

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### Purpose or Objective

The optimal frequency of prostate cancer image-guided radiation therapy (IGRT) has not yet been clearly identified. This study sought to compare the safety and efficacy of daily versus weekly IGRT.

### Material and Methods

This Phase III randomized trial recruited 470 patients with N0 localized prostate cancer, from 21 centers between June 2007 and November 2012. Total IGRT doses ranged from 70 to 80 Gy. Patients were randomly assigned (1:1) to two prostate IGRT control frequency groups: daily or weekly (Days 1, 2, and 3, then weekly). The primary outcome was 5-year recurrence-free survival (RFS). Secondary outcomes included overall survival (OS) and toxicity (CTCAE V.3.0). Post-hoc analyses included biochemical progression-free interval (BPFi), clinical progression-free interval (CPFI) and second cancer-free interval (SCFI).

### Results

Median follow-up was 4.1 years ( $Q_1 - Q_3 = 3.1 - 5.1$ ). There was no statistically-significant difference in RFS between the groups (hazard ratio [HR] = 0.81 [95% CI: 0.52 - 1.25];  $p = 0.330$ ). OS was worse in the daily control group versus the weekly control group (HR = 2.12 [95% CI: 1.03 - 4.37];  $p = 0.042$ ). Acute Grade  $\geq 1$  rectal bleeding was significantly decreased in the daily group (6%) versus the weekly group (11%) ( $p=0.014$ ). Late rectal toxicity (Grade  $\geq 1$ ) incidence was significantly lower in the daily control group (HR = 0.71 [95% CI: 0.53 - 0.96];  $p = 0.027$ ). BPFi was better in the daily control group versus the weekly control group (HR = 0.45 [95% CI: 0.25 - 0.80];  $p = 0.007$ ). The 5-year biochemical progression incidence rates were 9% [95% CI: 5 - 15] in the daily group and 21% [95% CI: 15 - 29] in the weekly group ( $p = 0.007$ ). CPFI was better in the daily control group (HR = 0.50 [95% CI: 0.24 - 1.02];  $p = 0.057$ ). SCFI was worse in the daily control group versus the weekly control group (HR = 2.21 [95% CI: 1.10 - 4.44];  $p = 0.026$ ). Second cancers occurred within a median of 31 months following randomization and were located in the pelvis in 18% of cases only.

### Conclusion

Compared to weekly control, daily IGRT control in prostate cancer significantly decreases the risks of recurrence and late rectal toxicity but is associated with an increased risk of second cancer.

### Award Lecture: Klaas Breur Award Lecture

### SP-0539 Biological Precision in Radiotherapy

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### Abstract text

Cancer genetics tells us that each person's cancer is as unique as their fingerprints, creating an opportunity for personalised treatment, but which has never been delivered. Our in-depth understanding of the biology of cancer has so far given rise to targeted agents of only

modest benefit: causing a reappraisal of the strategy of molecular drug development. The relative radioresistance of tumors is a major impediment to delivering curative radiotherapy, therefore, molecular targets for pharmacological manipulation of radiosensitivity would be highly desirable, but such a strategy depends upon exploiting tumor-specific targets, some of which, such as hypoxia in the microenvironment are well known, but many of which remain to be identified.

We have over the last ten years carried out a number of unique high throughput screens to determine tumor specific targets for radiosensitisation that affect both intrinsic and extrinsic radiosensitivity. From these screens we have identified a number of novel druggable genes that appear to offer tumor specific effects. A number of these will be illustrated, but of great interest has been the ability to develop such screens to target not only intrinsic, genetic or epigenetic, differences between tumor cells, but to extend such screening to identify what have been thought of as extrinsic, or microenvironmental effects.

Tumour hypoxia renders cancer cells resistant to cancer therapy, resulting in markedly worse clinical outcomes. To find clinical candidate compounds that reduce hypoxia in tumours, we conducted a high throughput screen for oxygen consumption rate (OCR) reduction and identified a number of drugs with this property. From this screen we have identified drugs that reduce tumour hypoxia in patients, thereby potentially increasing the efficacy of radiotherapy. We have also identified drugs that potentially can be modified chemically to increase their efficacy, generating novel intellectual property. The results of these screens will be presented in this talk.

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#### Symposium: Challenges in human resources in radiotherapy

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##### SP-0540 Human resources in radiation oncology: how to predict changing needs in a changing world?

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##### Abstract text

The ESTRO-HERO project has shown that there is a huge variation in equipment and staffing levels across Europe. A considerable variation also in delivered courses per year is evident among the highest and lowest staffing levels, reflecting the variation in cancer incidence and socio-economic determinants, as well as the stage in technology adoption along with treatment complexity and the different professional roles and responsibilities within each country. The data thus underpin the need for accurate prediction models and long-term education and training programs. How can the need for radiotherapy services be predicted? Basically, there are two ways to assess the need for radiotherapy on a regional or national level. The Epidemiologic Evidence-Based Estimation (EBEST) is a deductive method using literature survey of evidence and advanced cancer statistics to identify indications for radiotherapy. Epidemiologic data are used to estimate the frequency of each indication in the population of interest. In the Criterion-Based Benchmark (CBB), the actual use of radiotherapy in a well-defined area with optimal access and resources are taken as the benchmark against which all other regions or countries are measured. The HERO project has used the EBEST approach, i.e. combined population-based cancer incidence with evidence-based data on the effective utilization of radiotherapy to explore the optimum utilization of radiotherapy in Europe. For the forecast of

future needs, the epidemiological models are used to predict variations in tumor type and stages. The future need for equipment and staffing can then be estimated on a country level using the specific national infrastructure norms. The HERO analyses show that the optimal radiotherapy utilization benchmark is not met in the vast majority of countries, not even the most affluent and well-served countries. Despite improvements in equipment and staffing, there is today still a significant underutilization of radiotherapy in most European countries. Reasons may be lack of access to radiotherapy resources, but other factors including local and national treatment traditions, referral patterns, patient preferences, geography, co-morbidity, reimbursement rules etc. may also play significant roles. The current underutilization is unfortunately likely to continue in the future unless European countries start to perform long-term careful planning of future radiotherapy equipment and staffing needs. The anticipated significant increase in new cancer cases over the next years represents a real challenge to European radiation oncology. There is still a long way before every cancer patient in Europe will have access to state-of-the-art radiotherapy.

##### SP-0541 Tradition and innovation: reshaping the professional and scientific role of medical physicists in RT

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##### Abstract text

This presentation will not elaborate further on the so-called 2 souls of medical physics as it was nicely stated in an editorial of Radiotherapy and Oncology in 2015, referring to the difficult balance between clinical service and research. One might argue that more clinical-oriented departments attract more clinical-oriented physicists, and research-oriented scientists find their way into more research-oriented centres. The existence of a continuous spectrum ensures a proper place for each specific profile. The title of the presentation implies that a change is required, but do we really need to reshape the role of medical physicists in radiation oncology? The reason why Radiation Oncology has been evolving and continues to do so, is largely due to innovations and developments in physics. The role of medical physicists ("scientists" might be more appropriate as the term "medical physics" in radiotherapy covers a wide range of scientific skills) is largely related to their skills in joining disciplines and transferring new scientific developments into biomedicine and particularly in oncology. Cancer is not one disease, there is not 1 magic bullet for cure, and synergy between different disciplines has been and will remain to be a key issue. Medicine is becoming more and more personalized and Radiation Oncology has always been on the forefront of this evolution. As such, medical physics is evolving and adapting as it always has. Large randomized trials are being more and more questioned with insights in patient-specific and biologically relevant parameters. Complex and individualized treatments require more accurate *in vivo* dosimetry not only for legal reasons, but also because data mining, tuning radiobiology models and complex decision support systems rely on it. As input data becomes more accurate, it also becomes more complex and overwhelming, which inevitably introduces data mining and machine learning into our discipline. The need for automation and economical constraints add to the complexity of the discipline and impose new challenges. Does this mean we need to reshape the role of medical physicists in radiotherapy or is it a case in point that "medical physicists" have a crucial role in bringing new scientific insights and developments into the complex oncology field?