patients, preoperative radiotherapy appears to be a good option for breast conserving therapy.

OC-0392
Tumour characteristics associated with local relapse after hypofractionated radiotherapy in early breast cancer
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Purpose/Objective: There is a strong inverse association between the proliferation indices of early- and late-responding normal tissues and their sensitivity to radiotherapy fraction size. The aim of this study is to test for association between Ki67 index and the fractionation sensitivity of breast cancer. The hypothesis is that tumours with high Ki67 indices are relatively insensitive to fraction size and over-represented in tumours relapsing after hypofractionated radiotherapy.

Materials and Methods: Between 1986 and 2003, the START-P and START-A trials each tested 2 test dose levels of a 13-fraction regimen (3.0 vs 3.3 Gy & 3.0 vs 3.2 Gy fractions, respectively) in 5 weeks against 25 fractions of 2.0 Gy following primary surgery for early breast cancer. Primary tumour blocks of patients with local tumour relapse were collected for immunohistochemistry (IHC) for Ki67, HER2, ER, PR, CK5/6, EGFR, Geminin, Cyclin A, ATM, BRCA, PTEN and p53. A novel image-processing algorithm was developed to enable in silico alignment of serial tumor sections on a pixel-level and subsequent automated Ki67 scoring. For the initial Ki67 assessment all relapsed patients in the test arms were grouped together.

Results: From a total of 3646 patients entered into the START-P & -A trials, 261 local tumour relapses were recorded at a median follow up of 8.4 years (range 0.9-17.5) and 7.2 years (range 0.7-11.9), respectively. Blocks from 213 patients were recovered, of which 181 were evaluable by IHC. There was no significant difference in proliferation between tumours relapsing after conventional and hypofractionated radiotherapy, with mean Ki67 scores of 7.63 (95%CI: 5.06-11.5) and 5.33 (95%CI: 3.86-7.35), respectively. There was a positive correlation between Ki67 and Geminin scores (r=0.43, 95%CI 0.30-0.54, p<0.0001). The ongoing automated Ki67 scoring done in 41 patients so far has shown a high degree of correlation with manual scoring (r=0.76, 95%CI 0.60-0.6, p<0.0001). Based on unsupervised hierarchical clustering analysis of biomarker expression (bimodal data) patients were grouped mainly intoER/PR+, CK5/6 & EGFR+ and Ki67 high expressors, recapitulating known breast cancer subtypes. However, based on this 12-biomarker profile, a subgroup of patients enriched for recurrences in the different dose fractionation schedules cannot be identified.

Conclusions: An association between proliferative indices and fractionation sensitivity in breast tumours has not been demonstrated in the 2 trials analysed together, and adjusted analyses of any imbalances in tumour characteristics between trials will be presented.

Symposium: Advanced technology assessment: Economic evaluation of radiotherapy: Different approaches converging to a same answer?

SP-0393
The costs and benefits of radiotherapy: using treatment fractions to estimate radiotherapy costs and effects
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Radiotherapy is an essential part of cancer care. Successive studies have shown radiotherapy to be inexpensive and cost-effective. These studies are difficult to undertake and may not be applicable in different countries because of variations in work practices, wages and capital costs. A population-based model of radiotherapy demand and benefits could provide an estimate cost effectiveness if it was coupled to cost data. It could be updated simply by adding new cost or epidemiological data.

We have developed a model of every indication for radiotherapy that has allowed us to estimate that 48% of cancer cases in a Australian require radiotherapy at least once (http://tinyurl.com/pwkua34). It is possible to adapt the model to other countries by substituting the relevant proportions of cancer types and even stages for that country. The model has been expanded to estimate the number of fractions per indication and thus an average of 18 fractions is needed per course. We have also estimated the survival and local control benefit of radiotherapy at 5 years by tumour type. Using Markov modelling it is possible to calculate the number of Life Years Gained and thus we can calculate a survival benefit per fraction. By costing fractions in different countries it will be possible to estimate the cost per life year gained.

SP-0394
Cost-effectiveness of radiotherapy in Europe: a uniform solution for a heterogeneous context?
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Europe is characterized by its highly heterogeneous landscape with different cultures, traditions and languages. In the context of cancer care as well, large differences are observed in cancer incidence and survival, in economic aspects and available resources, in organization and funding of health care. Cost accounting and economic evaluation models should be developed that allow grasping this heterogeneity.

The ESTRO Health Economics in Radiation Oncology (HERO) project wants to provide a blueprint of the European radiotherapy landscape from an economical perspective. The aim is to support the individual European countries and their national radiotherapy societies in developing and sustaining an optimal radiotherapy service, in line with evidence-based
recommendations, yet tuned to the national context and the economic specificities of the country. The first work-packages of the HERO project have objectivized a large variation within European countries in resource availability and in actual needs for radiotherapy provision, related to the national cancer incidence. It also showed a remarkable lack of guidance for radiotherapy planning, with national recommendations mostly duplicating the available recommendations from international organizations or projects, without any attempt to streamline them to the needs of the individual country. Due to the growing awareness of resource limitations and tightening budgets, the weighing of costs and outcomes as performed in economic evaluations have become an integral part of the health resource allocation processes in many countries. Whereas cost-effectiveness data are typically required prior to the introduction of new drugs, they gradually also become more frequently requested to support radiotherapy financing. In order to make valid recommendations, the economic evaluations should however mimic the actual clinical and economic situation of the specific country. Yet, cost-effectiveness data from one country are not necessarily representative for another. The next step within the HERO-project is to develop a costing model that provides accurate radiotherapy resource cost data, based on the available resources, the cancer epidemiology and the radiotherapy practice of individual European countries. Time-driven activity-based costing, a cost-accounting method specifically developed to capture product complexity and variability, is highly suitable for that purpose. A final step will be to evaluate how these cost data can be combined with effectiveness data - derived from international studies but applicable to a country-specific environment - in an adaptable economic evaluation model, relevant for individual countries in the heterogeneous European context.

SP-0395
The equity gap in access to radiotherapy in the world. How do we close the divide?
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Abstract not received.

OC-0396
Identification of a microRNA signature associated with risk of distant metastasis in nasopharyngeal carcinoma
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Purpose/Objective: Despite significant improvement in locoregional control in the contemporary era of nasopharyngeal carcinoma (NPC) management, patients still suffer from a significant risk of distant metastasis (DM). Identifying those patients at risk of DM would aid in personalized treatment in the future. MicroRNAs (miRNAs) play many important roles in human cancers; hence, we proceeded to address the primary hypothesis that there is a miRNA expression signature capable of predicting DM for NPC patients.

Materials and Methods: The expression of 734 miRNAs was measured in 125 (Training Set) and 121 (Validation Set) clinically annotated NPC diagnostic biopsy samples.

Results: A 4-miRNA expression signature associated with risk of DM was generated by fitting a penalized Cox Proportion Hazard regression model to the Training data set (HR 8.25; p<0.001). This signature was subsequently tested in the Validation set, and maintained a significant relationship with DM (HR 3.2; p<0.01). In addition, multivariate analysis determined that this 4-miRNA signature was the strongest independent predictor when clinical factors were included. Finally, pathway enrichment analysis indicated that targets of the miRNAs comprising the final signature appear to be converging on cell cycle regulation.

Conclusions: This 4-miRNA signature adds to the prognostic value of the current ‘gold standard’ of TNM staging. In-depth interrogation of these 4-miRNAs will provide important biological insights that could facilitate the discovery and development of novel molecularly targeted therapies to improve outcome for future NPC patients.

OC-0397
A LAMP3 single nucleotide polymorphism associated with poor prognosis in breast cancer
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Purpose/Objective: Lysosome-associated membrane protein (LAMP)-3 is regulated by the unfolded protein response pathway. Our preclinical data suggest that LAMP3 plays an important role in autophagy induction during the response of breast cancer cells to various treatments and stress factors. We have shown that radiation therapy (RT), tamoxifen and hypoxia can induce LAMP3 and that high expression of LAMP3 is associated with resistance to RT and tamoxifen in breast cancer cells. Moreover, patients with high levels of LAMP3 mRNA had more locoregional recurrences. Here, we investigate the occurrence and clinical associations of a frequent non-synonymous single nucleotide polymorphism (SNP) in the LAMP3 gene (rs482912, Ile318Val) in 626 breast cancer patients.

Materials and Methods: A custom TaqMan® SNP Genotyping Assay targeted to our SNP of interest (rs482912) was used to assess its occurrence in breast cancer patients. We analysed the SNP’s association with several clinical factors by Pearson Chi-square tests, and performed Kaplan-Meier survival and Cox regression analyses to investigate a relation with locoregional control.

Results: In our cohort, the minor allele frequency for the LAMP3 rs482912SNP was 0.718, which is similar to the frequency in the European population. The SNP was not associated with menopausal status, type of operation, use of