PO-0755
Direct cost associated to breast cancer radiation therapy
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Purpose/Objective: Historically, breast-conservation therapy consisted of lumpectomy followed by 6-7 weeks of whole-breast radiation therapy (WBRT). More recently, alternatives to WBRT have been evaluated. These include hypofractionated WBRT, and partial-breast irradiation (PBI) through external-beam, brachytherapy, or intraoperative RT (IORT). We evaluated the direct cost associated to the different RT options.

Materials and Methods: We performed a cost analysis among: (1) 3-dimensional conformal RT (3DCRT) using a conventional fractionation (33 sessions [25 for the whole breast and 8 for the boost]); (2) Hypofractionated 3DCRT (23 sessions [15 for the whole breast and 8 for the boost]); (3) PBI delivered using: 3DCRT, high and low dose rate brachytherapy (HDR and LDR, respectively) and intraoperative RT (IORT). Treatment costs included: fractions number, hospitalization (i.e. LDR brachytherapy), consults (initial consult and weekly visits during treatment; nurse consults; anesthesiologist if needed), radiological examinations (i.e. portal verification films, planning computed tomography scan), blood tests, and dosimetry calculation. No costs were considered for systemic treatments, post-RT follow-up, transportation, accommodation, or meals. Prices of treatment and patient support were obtained from the last update of the authorized regional government agencies (BOJA 210; October 2005) at regular official prices. According the Spanish Association of Public Health Care Euros, the prices were updated until 2012 increasing the 3% per year to the total amount calculated.

Results: The duration of radiation treatments were 7 and 5 weeks for the conventional fractionation and the hypofractionated 3DCRT, respectively. Radiation was given in 1 week for the PBI delivered by 3DCRT or HBR brachytherapy and IORT, respectively. Treatment cost for conventional fractionation 3DCRT was 6,518,81€, whereas the hypofractionated regimen using the same technology cost was 4,718,46€. PBI costs were 3,078,60€, 4,483,49€, 4,075,36€, and 7,418,46€ for 3DCRT, LDR brachytherapy, HDR brachytherapy, and IORT, respectively (Table).

Conclusions: PBI treatment administration appears to be the more economic option, being the 3DCRT the cheapest technique. This treatment modality seems to be more convenient for elderly patients, especially in situations of difficult access to treatment delivering facilities. Multidisciplinary teams offering breast conservation to women with early-stage breast cancer should consider accelerated radiation regimens offering comparable therapeutic benefit with use of fewer Public Health Care Euros.

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Pursuing the methodology toward comprehensive evaluation of emerging radiation therapy innovations
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Purpose/Objective: To evaluate the feasibility of comprehensive evaluation of emerging radiation therapy (RT) innovations. This report presents the survey results of Radiation Oncology (RO) Physicians’ views in regards to the current evaluation process that is performed prior to the widespread implementation of RT innovations.

Materials and Methods: An online survey in English language was sent via e-mail to RO Department Heads of randomly selected centers to represent North/South American, European, African, Asian and Australian centers with a request to forward it to their RO Physicians. The survey questionnaire consisted of 20 questions and was created using the QuestionPro Online Software. Statistical analysis was done using Banner/Pivot Tables and Cross-Tabulation of different variables. P-values were calculated using Pearson’s Chi-Squared Test. This survey report represents the first phase of this project. During the second phase, an evaluation protocol software using Head and Neck module will be generated and sent online with a feedback questionnaire to be reviewed by RO’s from various international cancer centers.

Results: The online survey was viewed by 143 respondent. 121 respondent have completed the survey (84.62% Completion Rate). The majority (39%) were RO Physicians with 5 or more years of practice and 81.8% were from academic centers. 60% of respondents think that emerging RT technology innovations currently are not appropriately evaluated prior to widespread implementation. Also, 82% think that there should be a mandate to have more comprehensive evaluation prior to widespread implementation of these innovations. 83.5% think that vendors should be invited to provide logistical support to such comprehensive evaluation process. Years of experience were the only statistically significant variable (P-value=0.004) in regards to the respondents’ views toward the current evaluation process. 71% of Junior and 54% of Senior RO Residents think that the current evaluation process is appropriate versus 28% of Senior RO Staffs, 33% Junior RO Staffs and 25% RO Fellows. The surveyed potential advantages/disadvantages of the proposed comprehensive mandatory evaluation process are available to be presented at the conference along with the evaluation protocol database entry points.

Conclusions: While we are not in any way hamstringing creativity and innovations of Radiation Therapy Technology, we should strive for rigorous standardized post-marketing evaluation of any promising innovation prior to its widespread implementation. Any mandatory post-marketing comprehensive evaluation process should be carefully performed aiming to avoid slowing down such innovations or increasing its costs. This will help to reach the target goals of improving patients care and the utilization of healthcare resources without slowing down RT innovations or increasing their cost. The second phase of this project includes creating a software that takes these considerations into account.

PO-0757
The use of Failure Mode Effect Analysis (FMEA) to enhance quality in a busy radiotherapy setting
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Purpose/Objective: Delivering on quality in radiotherapy is a complex task. Colleagues, patients, administrators and tax payers seek continual quality improvement. Such demands require radiotherapy professionals to be committed to constantly enhancing the service they provide. The drive to provide safer, more effective, more efficient and more timely services is the goal of the modern radiotherapy clinic. Failure Mode Effect Analysis (FMEA) is a technique of systems engineering borrowed from large scale industrial processes. Its use in radiotherapy has recently been championed by ICRP 112 and its use in radiotherapy has recently been championed by ICRP 112 and by the formation of a task group of the American Association of Physicists in Medicine (AAPM TG 100). The application of FMEA in a clinical radiotherapy environment is described in this work. The objective is to assess the effectiveness of FMEA in achieving quality improvement in radiotherapy.

Materials and Methods: Using the conventional FMEA methodology this project consisted of four distinct steps as follows: 1) Process Mapping - a detailed process map was assembled by multidisciplinary team. This map identified 9 distinct nodes and over 100 sub-nodes of activity which detailed the radiotherapy process from initial imaging to first treatment. 2) Identification of Failure Modes (FM) - comprehensive analysis of where the process could fail based on a detailed analysis of the process map. 3) Quantification of FM - risk rating of FMs by analysis of their severity, probability of occurrence, and level of detectability. This

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step uses the Risk Priority Number (RPN) which is a product of relative indices of occurrence, detectability and severity.

4) Corrective re-design - process re-engineering to remove stresses from the system and reduce the likelihood of recurrence.

**Results:** A complex process map was produced and over 40 potential FMs were identified. In the system, RPN analysis identified 11 FMs which were rated sufficiently highly to initiate corrective re-design. This involved major initiatives such as ensuring the process was completely paperless, conduction of staff training sessions to promote independent checking and the purchase of additional equipment to reduce the incidence of incorrect patient set up. More minor re-design initiatives involved increasing the incidence of patient identification checks and ensuring multiple assessment of pregnancy status throughout the process.

**Conclusions:** This study has indicated that FMEA can be applied in the RT setting. Although an ever evolving process FMEA has identified scope for improving the RT process, strengthened the risk management matrix and enabled the evolution of a bespoke QC programme designed on the basis of prospective analysis and quantification of risk. Much further work is required in this area such as tighter specifications of RPNs, and a reduction in the beauracratic load however it is felt FMEA is a valuable and rapidly developing quality tool for radiotherapy.

**POSTER: CLINICAL TRACK: OTHER TUMOUR SITES**

**PO-0758**

**Modelling radiotherapy escape using BRCA1/2-def mice mammary tumors and Image-guided irradiation**

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**Purpose/Objective:** To investigate responses to clinically relevant radiotherapy regimens in new generation mouse models for BRCA1/2-deficient breast cancer using a preclinical system for image-guided irradiation.

**Materials and Methods:** Radiotherapy interventions were carried out using a small-animal dedicated Cone-Beam CT (CBCT) equipped micro-irradiator. A dose-response (i.e. Tumor Control Probability, TCP) relationship was determined using various fractionated treatment regimes (i.e. 2Gy, 4Gy, 8Gy per fraction) in the BRCA1 model. In addition, radiosensitivity of the other models was determined. For this purpose, the tumors were measured by caliper and CBCT. Metastatic spread was investigated by CBCT and routine pathology of inner organs. We are currently harvesting residual and relapsing tumors that escaped radiotherapy control to determine whether these contain stably radioresistant cells. Similarly, tumor specimens of metastatic lesions are reimplanted and irradiated to determine the radioresensitivity. Ongoing assays are evaluating DNA damage and repair, epithelial-mesenchymal transition (EMT) and gene expression profiling.

**Results:** After a follow up of 6 months we observed a dose dependent TCP relationship. According to the Linear-Quadratic Model using 3Gy, the D50 and m were 84Gy and m=0.5, respectively (Fig). The optimal $\alpha/\beta$ ratio to recalculate the physical dose into a biologically equivalent dose (as given in 2 Gy per fraction) was 3 Gy. As expected, the BRCA1/2-deficient carcinomas were highly sensitive compared with the BRCA proficient carcinomas. In contrast, BRCA2-deficient tumors that had undergone EMT only responded moderately to radiotherapy. Despite their high sensitivity, most BRCA1/2-deficient carcinomas were not eradicated, and eventually relapsed (Fig). Although most recurrent tumors responded again to radiation, the response durations were shortened. Moreover, some recurrent tumors escaped radiotherapy control. As an alternative way to escape local radiotherapy control, we observed the occurrence of distance metastasis in about 20% of mice.

**Conclusions:** Using dedicated preclinical image-guided irradiation techniques we present here that genetically engineered mouse models for BRCA1/2-deficient breast cancer are useful for the study of radiotherapy response. Our data strongly suggest that we may have a method to develop radiotherapy-resistant tumours which will be helpful to tackle the clinical problem of radiotherapy resistance. In particular, therapeutic approaches to increase radiosensitivity and prevent metastasis formation (e.g. PARP inhibitors) can be tested in these models. Moreover, we are investigating the role of hypoxia and DNA damage repair and targeted agents for radioresistance. Our hope is that these models may help to identify new therapeutic strategies that could guide clinical trials in the future.

**PO-0759**

**Factors affecting the radiation reactions in cancer patients previously subjected to chronic irradiation**

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**Purpose/Objective:** Determination of the main factors affecting the development of radiation reactions in the group of patients with chronic exposure. The possible impact of the absorbed dose received as a result of chronic radiation exposure associated with the activities of the plant Mayak, the incidence and severity of radiation reactions during radiotherapy.

**Materials and Methods:** We have carried out a retrospective analysis of medical data of patients treated with external beam radiotherapy for solid tumors of various localizations. Study group comprised 89 patients who had an indication on chronic radiation exposure history. 182 patients of the control group prior were not been exposed to radiation. Patients of study and control groups were matched for age, sex, diagnosis and treatment. Assessment the frequency, severity of radiation reactions and complications was performed.

**Results:** It was shown that the quantity of absorbed dose from chronic irradiation has no significant effect on the incidence and severity of radiation reactions. The frequency of radiation reactions did not differ significantly ($p=0.957$); in the study group was 59.6% (53 patients), in the control group - 60.3% (108 patients). The distribution of reaction severity did not differ significantly between groups ($p=0.176$). However, the study group was dominated by the Grade II reactions (64.15%), while in the control group Grade I and Grade II reactions distributed almost equally - 51.4% and 48.6% respectively. In some cases symptoms of the reactions caused the need to interrupt treatment. The number of breaks was significantly higher in the study group - 10 (11.2%) than in control - 7 patients (8.8%) ($p=0.018$). There was statistically significant difference in the dynamics of the process ($p=0.048$), indicating a lower frequency of the positive effect of radiotherapy in previously irradiated patients. There were no statistically significant effect on the frequency of radiation reactions of absorbed doses to red bone marrow (CMC) ($p=0.534$) and soft tissue ($p=0.359$). The dose to the red bone marrow had no effect on the considered parameters: the treatment completion ($p=0.226$), the frequency of breaks ($p=0.777$), dynamics ($p=0.88$).

**Conclusions:** These data suggest that the main factors affecting the frequency of radiation reactions in cancer patients with chronic radiation exposure history, similar to those in patients without prior exposure to radiation. However, the detected changes in the severity of the reactions, dynamics of the process may be indicative of changes in radiosensitivity in patients previously exposed to chronic irradiation. Incorporation of these features in the radiotherapy planning will help to optimize a treatment plan, to reduce the incidence and severity of reactions, thereby improving the quality of life in cancer patients.