Conclusion: RT is highly effective for refractory degenerative joint diseases. Prognostic factors for outcome can be established. Due to minimal side effects and low costs, RT represents an excellent treatment compared to conventional methods of treatment and surgery in the chronic disease. This study confirms by objective criteria the anti-inflammatory efficacy of low dose RT

EP-1479
Integration of a minituarized linear accelerator in an 20 year IOERT expert institution
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Purpose or Objective: Hospital General Universitario Gregorio Maranon has a long-standing tradition of IOERT (Intraoperative electron Radiation Therapy), with over 1600 procedures in its 20 year history. Since december 2013, a minituarized linear accelerator (LIAC) started to operate in our center. We describe the 22 months technical and clinical experience with LIAC in our consolidated IOERT program.

Material and Methods: A review of technical and surgical parameters of IOERT procedures using LIAC was performed from December 2013 to October 2015.

Results: From december 2013 to october 2015, 222 procedures in 185 patients were performed (200 procedures with LIAC, 22 transported to a fixed lineal accelerator). Cancer types treated were 64 oligorecurrences / oligometastases, 34 breast cancers, 44 rectal cancers, 42 sarcomas, 6 pancreatic adenocarcinomas, 4 esophageal neoplasms and 6 other cancer types. The treated anatomic sites included 100 cases in pelvis, 40 in abdomen, 25 in limbs, 34 in breast and 1 in thorax. Relevant operational data included 39 days with more than 2 procedures in the same working day (22% of total days). Six different applicator sizes were selected (range 4-10) with 4 beveled ends (range 0-45). Selected energies ranged from 6 to 12.

Conclusion: LIAC is a versatile technology able to be incorporated to expert IORT institutions promoting efficient action with operative benefits in terms of availability of IOERT components for cancer patients.

EP-1480
A comprehensive analysis of immuno- and immunoradiotherapy trial design developments from 2000-2014
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Purpose or Objective: There has been a rapid growth in the number of immuno- and immunoradiotherapy trials over the last few decades. Long term durable responses occur, but only in a subset of patients. As yet no accurate method of identifying those patients most likely to benefit has been identified. The factors behind non-response are unclear but may include 1) inherent characteristics of the tumour, 2) factors influencing immunogenicity such as tumour burden and previous treatments and 3) clinical trial design. By performing a cross sectional analysis of registered clinical trials investigating agents thought to stimulate T-cells we aimed to detect trends in these factors. In particular we aimed to assess the extent to which trials sought to develop and identify novel biomarkers of response to immunotherapy.

Material and Methods: A pubmed literature search was conducted to establish a list of known T cell checkpoints, co-stimulatory receptors, ligands, and the antibodies targeting these. These search terms were entered into clinical trials.gov on October 11, 2014. Study details were downloaded as datasets for review by two independent assessors.

Results: We identified a total of 350 trials of immunomodulatory antibodies targeting PD-1, CTLA4, PD-L1, PD-L2, LAG3, B7-H3, CD137, OX40, CD27 and GITR. A longitudinal analysis by trial registration date shows a steady increase in the number of trials using immunostimulatory antibodies. As some cancer types are thought to be more immunogenic, we looked at the spread of trials by cancer type. Unsurprisingly, melanoma trials represent the largest proportion, but there has been a shift towards testing immunostimulatory antibodies in cancers that are considered less immunogenic with a significant increase in trials in NSCLC when comparing trials registered between 2000 and 2007 and those registered between 2008 and 2014. Only 39% of trials measured a dynamic immune endpoint as a specified outcome. T and B cell number or function were the most common markers analysed. However there was a significant increase in the measurement of PD-L1 expression in recent years.

Conclusion: This analysis provides comprehensive data on the rapid growth of immunotherapy trials and highlights that despite the multiplicity and variability of potential dynamic biomarkers available, there has been a poor uptake. Whether the future of immunotherapy is not in doubt, biomarkers are essential to understand the considerable lack of response and help guide further trial efforts.

EP-1481
Toxicity of concomitant application of radiotherapy with „new targeted therapies”
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Purpose or Objective: New targeted therapies (nTTs) are increasingly used in virtually every type of cancer. On the other hand radiation therapy (RT) is frequently applied in the curative and palliative setting of cancer treatment, confronting clinicians more and more with the problem, weather a previously initiated nTT-therapy could be continued during RT. The aim of this systematic literature analysis was to evaluate the toxicity of concomitant application of RT with nTTs in a qualitative descriptive manner.

Material and Methods: Clinical studies comprising concomitant application of RT with EGFR-, VEGFR-, HDAC-, proteasom-, BRAF-, m-Tor- or immune-checkpoint-inhibitors were eligible. Using fixed search terms 215 publications were identified including more than 6000 patients. Forty-eight studies analyzed combinations of nTTs with ZNS-RT including 1164 patients, 45 with head and neck-RT including 2390 patients, 59 with thoracic RT including 1647 patients, 33 with abdominal RT and 30 with pelvic RT including 492 and 1008 patients respectively.

Results: In most cases combined application produced no additional toxicity or a slight increase of the already known toxicity profile. Scarcely, however, combination of RT with nTTs resulted in serious side effects. These toxicities comprised tracheo-bronchial fistulas or GI-bleeding for combinations of thoracic or abdominal/pelvic RT with VEGF-receptor-inhibitors, recall phenomena in combination of RT with tyrosinkinase inhibitors e.g. erlotinib and severe mucositis, dermatitis or paraplegia (case report) when combining RT with ipilimumab. For the majority of these
serious side effects no predictive risk factors could be isolated.

Conclusion: The currently available data seems to be not adequate to give a general recommendation, on weather RT could be combined with nTTo in clinical routine. If application is carried out on an individual basis it should be done under close clinical surveillance. Multicentric observational studies are needed to address this clinical relevant problem.

Electronic Poster: Basic dosimetry and phantom and detector development

EP-1482
Improving accuracy of radiochromic film dosimetry system using control film piece
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Purpose or Objective: Over the years, radiochromic film became a reference dosimetry system of choice for two-dimensional dose distribution measurements with acceptable accuracy and uncertainty in both clinical and research applications. Nonetheless, response of the film might be influenced by factors other than irradiation (humidity, extreme temperature and/or exposure to UV light) that could lead to decreased measurement accuracy. We investigate the use of a control film piece, which should compensate for the film response changes other than radiation.

Material and Methods: Response of EBT3 film was measured in terms of net transmittance calculated using green channel from 48-bit RGB image of film pieces scanned with Epson Expression 10000 XL flatbed scanner. We established a calibration curve for the radiochromic film dosimetry system in a dose range up to 20 Gy. Then, we irradiated “control” film pieces to several known doses from 0.05, to 1 Gy, as well as five film pieces of the same size to “unknown” doses of 2, 5, 10, 15 and 20 Gy. Impact of correcting measured (“unknown”) doses using “control” film pieces were investigated in terms of both gain in the accuracy and at the same time loss of uncertainty of such determined dose. Depending on a dose range, two approaches of incorporating control film piece were investigated. In a signal based method, response of the control film piece is subtracted from the measuring film piece and the final change in response is converted into dose using calibration curve. In a dose based method, both readings of measuring and control film pieces are converted into the dose using same calibration curve followed by subtracting the control film piece “equivalent” dose from the dose obtained with measuring film piece.

Results: Figure 1 summarizes results of our investigation into trade-off between gain in accuracy and loss in uncertainty when the control film piece is used, and we found that both are dependent on dose level measured. For dose values above 10 Gy, the increase in accuracy of 3% results in uncertainty loss of 5% by using dose corrected approach, whereas the measured film response corresponded to 2% of the dose response registered with measuring film piece. At lower doses and signals of the order of 5% (measured by control film piece) we observed an increase in accuracy of 10% with a loss of uncertainty lower than 1% by using the corrected signal approach.

Figure 1: Trade-off using control film piece: percentage uncertainty loss and percent accuracy gain for signal corrected (top left) and dose corrected (top right) approach as a function of measured doses for various dose measurement levels, absolute error for signal corrected (bottom left) and dose corrected (bottom right) approach. I: representation guide for the eye.

Conclusion: Use of the control (un-irradiated) film piece for dose measurements in reference radiochromic film dosimetry is highly recommended. At lower doses, the signal based method should be used, while at higher doses the dose correction method seems to be more appropriate. However, final incorporation of the signal registered by the control film piece into dose measurement analysis should be a judgment call of the user based on a tradeoff between deemed accuracy and acceptable uncertainty for a given dose measurement.

EP-1483
Reference dosimetry of FFF MV photon beams: a correction for intra-Farmer ion chamber dose gradients
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Purpose or Objective: To estimate and correct the systematic bias which results from the intra-chamber dose gradients when a Farmer ionization chamber is used for reference dosimetry (TRS 398, IAEA 2000) in flattening-filter-free (FFF) MV photon beams.

Material and Methods: An intra-chamber dose gradient correction factor (K_Icdg) of the charge reading of a Farmer ionization chamber, when used for reference dosimetry (TRS 398, IAEA 2000) in flattening-filter-free (FFF) MV photon beams, is proposed. This is achieved through a user intercomparison of the Farmer ionization chamber with a small volume (~ 0.1 cm³) ionization chamber, and by estimating the inaccuracies of this intercomparison. Further, the factor K_Icdg is theoretically developed in terms of the corrections for both volume averaging effect (P_vol) and charged particle fluence perturbation (P_fl). The factor P_vol is then estimated as the ratio of the active length (L) of the Farmer ionization chamber (L= 24 mm) over the integral, computed on L, of a high-resolution FFF transverse dose profile (Figure 1). Once K_Icdg and P_vol are known, P_fl is finally deduced.

Results: The estimated overall standard uncertainties on the absorbed dose to water determination in reference conditions, for 6 MV and 10 MV FFF beams, were 1.5 % for the small volume ionization chamber (30013™, PTW), and 1.4 % for the K_Icdg-corrected Farmer ionization chamber (30013™, PTW). In the latter case, the added uncertainty from the measure of K_Icdg was balanced by the higher long-term stability of the Farmer ionization chamber. From four distinct dosimetry sessions on a TrueBeam™ (Varian Inc.) linac, mean (sd) values for K_Icdg equal to 1.0024 (0.0003) for 6 MV-FFF and 1.0056 (0.0003) for 10 MV-FFF, were estimated. Similarly, P_vol equal to 1.0030 (0.0001) for 6 MV-FFF, and to 1.0064 (0.0004) for 10 MV-FFF, respectively, were measured.