The need for biology in future radiation oncology
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Abstract not received.

SP-0595  Who does what: The increasing role of the RTT
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Given the wide range of education programmes internationally, what is included within the standard scope of practice of Radiation Therapists (RTTs) is highly variable. The responsibilities of RTTs are primarily based on historical definitions of roles and typically refer to a basic set of clinical competencies. However the professional boundaries of RTTs in modern radiotherapy are being challenged and redefined.

Modern radiotherapy cares for a population of increasing age, with techniques of increasing complexity. The need for improved efficiency, whilst maintaining a high quality service has resulted in a demanding work environment for the entire multidisciplinary team. As such, RTTs are finding themselves taking on increased responsibilities in a wider range of clinical tasks. RTTs today may be involved in complex dosimetry and planning, quality assurance, use sophisticated image guidance equipment and also assess and triage patients for toxicity assessment. The RTTs involvement in education and research activities also continues to grow; from simply supporting their colleagues to the actual management of clinical trials, as an example. In an attempt to formally recognise this, a number of countries have explored the position of Advanced Practice or Specialist RTTs. This concept is more than a change in specific duties, but a greater level of understanding and autonomy in their work practice. What was once considered advanced is now considered standard and as such, the definition of these roles is also ever evolving. What is widely recognised, however, is the success of such roles is dependent on a professional culture that supports the development of RTTs and an education system in place to facilitate this progression.

Whilst the economic impact of such initiatives is difficult to quantify, it has been reported that through role expansion of the RTT there has been a decrease in patient wait times with improvements in access to care and development of innovations in clinical practice. Furthermore, this shift in practice has allowed for not just a more efficient use of RTTs but has also enabled Radiation Oncologists, Medical Physicists and Nursing staff to focus their efforts on development within their own disciplines.

Modern radiotherapy is demanding and as such the role of the RTT is dynamic. As our workforce grows and changes so too must our education programmes in order to meet the needs of the professional radiotherapy community.

Symposium: New targets and evaluation in model systems and early trials

SP-0596  New models to study therapeutic targets in tumours and normal tissues
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New technologies for the radiation treatment of small animals allow preclinical studies using orthotopic xenograft models with radiochemotherapy that more closely mimic clinical studies. We have used an XRad 225Cx small animal irradiator/imager to deliver fractionated dose treatment and chemotherapy to early-passage orthotopically growing human cervix cancer xenografts in immune-deprived mice. This model allows assessment of both primary tumour growth and metastases occurring in the para-aortic lymph nodes. Irradiation treatment was delivered to tumours of 5-8 mm diameter growing in the cervix of mice using an 8-beam protocol with imaging of the target immediately prior to each fraction. The treatment plan allowed for a 1-2 mm margin around the imaged tumour target. The radiation treatment (15-20 x 2Gy fractions delivered 5 days/wk) was combined with weekly cisplatin (4 mg/kg/wk) to match current external beam treatment procedures for cervix cancers. Tumour growth delay analysis was performed using the imaging features of the irradiator to assess tumour size as a function of time during and after the treatment. There was limited response of the primary tumour to treatment with cisplatin alone but significant response to fractionated radiation treatment, which was enhanced when combined with cisplatin (CRTx). Additional combination treatment with either AMD3100, a drug that blocks the interaction of the CXCR4 chemokine receptor with its ligand CXCL12, or with Hedgehog pathway inhibitors, further enhanced the treatment response of the primary tumours. Lymph nodal metastases in the aortic chain were also significantly inhibited. No significant short-term toxicities have been encountered to date during these studies, in particular there is no enhancement of the response of small intestinal stem cells as assessed using a G1-tract clonal assay.

SP-0597  Nitroglycerin as a sensitizer in the treatment of non small cell lung cancer: from cells in vitro to phase 3 trial
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Nitroglycerin, a nitratic oxide donor agent, reduces the expression of hypoxia-inducible factor-1α (HIF-1α) and could be a normalizer of the tumor microenvironment. Both factors are associated with chemo-radio-resistance. Adding nitroglycerin to the combination of vinorelbine plus cisplatin has been reported to improve the overall survival (OS) of Asian patients with stage IIIIB/IV non-small cell lung cancer (NSCLC) (Yasuda et al. J Clin Oncol. 2006). Several trials tried to confirm that result with contradictory results. A Mexican phase 2 trial concluded that the addition of nitroglycerin to induction chemotherapy and concurrent chemoradiotherapy in patients with locally advanced NSCLC has an acceptable toxicity profile. We hypothesize that the contradictory results obtained were a consequence of the fact that a) we do not know the mechanism of action of nitroglycerin and b) the fact we do not have a biomarker to select the right patient. We further hypothesize that the patient with an hypoxic tumours are more likely to benefit from nitroglycerin patch and that nitroglycerin would act as inhibitor of oxidative phosphorylation by inhibition of complex 1. We tested these two hypothesis respectively with
a window of opportunity trial “hypoxia scan-nitroglycerin - hypoxia scan” (ClinicalTrials.gov Identifier: NCT01210378) and in the lab with a cellular respiration assays measuring Oxygen consumption (OCR) and extracellular acidification (ECAR) using Seahorse XF96 extracellular Flux analyser. Currently 19 patients have received their baseline HX-4 scan of which 14 patients received a second nitroglycerin scan as well. The median interval between the baseline and nitroglycerin scans was 4.5 days (range 2-7 days).

We found that Nitroglycerin significantly decreases the hypoxic fraction in all investigated non-small cell lung cancer tumours and metastatic lymph nodes. Our lab work demonstrate that nitroglycerin has an inhibitory effect on mitochondrial respiration which by decreasing oxygen consumption increase the availability of oxygen and decrease hypoxia.

This promising result encourages further investigation of nitroglycerin as a radio-sensitizing agent using hypoxia imaging as biomarker for selection.

SP-0598
Cilengitide in continuous infusion with radio-chemotherapy in stage III NSCLC: A phase I clinical trial
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Introduction: We have previously shown that αvβ3 integrins control radioresistance, hypoxia and angiogenesis and that co-expression of FGF-2 and αvβ3 integrins in the tumors of patients treated with exclusive radio-chemotherapy for stage III non-small lung carcinoma (NSCLC), was associated with a worse local control, suggesting that inhibition of αvβ3 integrin could induce a radiosensitization of such tumours. We designed a phase I trial associating the specific αvβ3/αvβ5 integrin inhibitor Cilengitide with radio-chemotherapy in patients with stage III NSCLC.

Patients and methods: A standard 3+3 dose escalation design was used. Cilengitide was given in continuous infusion starting 2 weeks before and then during the whole course of the radio-chemotherapy (66 Gy combined with a Platine-Navelbine regimen), and then at a dose of 2000 mg twice a week in association with chemotherapy. Planned Cilengitide continuous infusion dose levels were 12, 18, 27 and 40 mg/h. PET-FDG and CT scan were performed before and then after the first two weeks of Cilengitide administration and then 2 months after the end of radio-chemotherapy. Patients were followed by CT scan. Toxicity for DLT was assessed during combined treatment and until 1 month after. Clinical response on CT scan and TEP was evaluated according to RECIST and PERCIST criteria.

Results: Fourteen patients were included between March 2010 and July 2013. Eleven patients were evaluable for DLT. No DLT was observed at level 0, 1 and 2. One DLT, a tracheo-bronchial fistula was reported at the 40 mg/h dose.

No relevant adverse event related to Cilengitide (7 grade 1 and one grade 2) was observed on the whole population. Among 11 patients evaluable for efficacy, 9 patients presented a partial response and 2 a stable disease. At 12 months after the end of radio-chemotherapy, 4 patients presented a progressive disease. At PET evaluation 2 months after radio-chemotherapy, 4 patients had a complete response and 4 patients had a partial response.

Conclusion: Cilengitide given continuously with radio-chemotherapy was well tolerated and shows encouraging clinical results, suggesting that targeting αvβ3 integrin continuously during radio-chemotherapy in NSCLC is a promising approach to treat this disease.

Symposium: Revisiting low and medium energy beams: focus on dose measurement, calculation and QA

SP-0599
Commissioning and QA of skin electronic brachytherapy applicators
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Moulds and Flaps are typically used on superficial skin brachytherapy for Planning Target Volume (PTV) up to 5 mm depth. In the cases of small and flat PTV, the use of superficial skin Applicators is an efficient solution because they shield the surrounding healthy tissues. In contrast to electrons beams applications (where bolus and specific dosimetry is required), treatment planning and delivery is simpler.

There are radionuclide-based HDR Ir-192 Applicators, as the Leipzig (Varian and Elekta) and Valencia (Elekta) ones. The Valencia Applicators are a modification of the Leipzig ones where a flattering filter has been added. Consequently, lateral homogeneity, penumbra, and useful beam are improved. However treatment time becomes longer.

The electronic HDR brachytherapy surface applicators offer an alternative to external beam electrons and HDR radionuclide brachytherapy modalities. There are currently two systems being used clinically: Xoft Axxent® (iCad) with 50 kVp which has been in use since 2009, and Esteya® (Elekta) with 69.5 kVp which has been released in 2014. We will discuss in this presentation our experience with the Esteya Unit, regarding commissioning, QA and clinical implementation.

Esteya is a new brachytherapy Unit designed to obtain dose distributions similar to Valencia App with an X-ray source of 69.5 kVp. It has an adjustable arm and a set of interchangeable circular applicators of different diameters (10 mm, 15 mm, 25 mm, and 30 mm). Once overall absorbed dose, number of fractions, prescription depth and applicator size are selected in the console treatment planning system, the system presents automatically the treatment time. Compared with the Valencia Applicators there are improvements in penumbra, treatment time, gradient on PTV and leakage.

The following aspects of commissioning will be discussed on this presentation:

Timer: Reproducibility, accuracy and linearity (combined with mA)

Flatness, symmetry and penumbra: Using radiochromic films and high spatial resolution array SRS1000 (PTW, Germany)

HVL: Diode vs. ionization chamber detectors. Comparison of different set-ups