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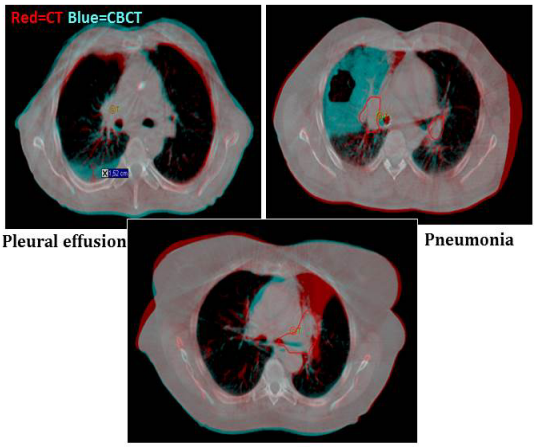

Symposium: Around organs / combination therapy: Gut

SP-0029

GI consequences of cancer treatment: the past, the present and the future: a clinical perspective

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Toxicity is an inevitable consequence of cancer treatment. While patients want curative treatment if possible, quality of life issues have been somewhat neglected in the race to improve survival. Patient reported outcome measures (PROMS) confirm that most routinely used clinical scoring systems fail to identify important toxicities and as a result the frequency, severity and impact on patients' lives of chronic GI consequences of cancer therapies has historically not been fully recognised by clinicians. Nor has it received the attention that it deserves in terms of research. Yet the iatrogenically driven morbidity of cancer treatments and especially radiotherapy is an important human model of GI disease and has already yielded new insights which can be applied to benign and malignant diseases.

In the last 20 years, a largely unheralded but spectacular revolution in understanding why toxicity develops, how it should be identified, measured and managed has gathered speed. Inaccurate terminology describing toxicity in the past has significantly hindered progress. It is now recognised that toxicities rarely affect just one organ system and the concept that toxicities after radical treatment are a progressive disease, Pelvic Radiation Disease, have helped formulate more productive treatment approaches and understand future priorities. Clinical studies now show that applying this new understanding allows much GI toxicity previously widely regarded as incurable to be ameliorated.

In addition, biomarkers of radiation toxicity – fibrotic markers which can be measured in blood are the most promising – offer a much more accurate method of detecting toxicity than the current approach of defining toxicity by a change in symptoms and this is starting to allow new methods of preventing toxicity, to be targeted more accurately.

It is also increasingly understood that the "consequential effect" has a critical role in the development of chronic toxicity and that it is driven by factors beyond the control of the oncologist. One of the most important of these is the composition of the gut microbiota; another is the role of the immune system. Introducing techniques already used by other disciplines to manipulate these factors will deliver future great rewards in terms of reducing chronic toxicity.

GI toxicity is a major limiting factor to the advance of oncological treatments. Many new solutions have emerged but require the harnessing of a multidisciplinary approach in a way that oncology has rarely used up to this point.

SP-0030

Having guts: saving the organ

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Intestinal radiation injury may severely hamper quality of life during and after treatment of abdominal tumors. Even though novel technical advances in treatment delivery have enabled more selective irradiation of the tumor, normal tissue radiation injury remains the most important dose limiting factor of radiotherapy. Hence, there is an urgent need for agents that can be administered during radiotherapy to prevent and/or reduce radiation-induced intestinal injury. These agents should of course not hamper the anti-tumor effect of radiation and, ideally, even improve radiation-induced tumor cell kill.

Pre-clinical studies have shown that the novel Somatostatin analogue Pasireotide effectively reduces radiation-induced intestinal injury by preventing post-irradiation pancreatic enzyme-dependent intestinal auto-digestion. In our experiments Pasireotide was shown to preserve the intestinal mucosal surface and to prevent intestinal bacterial translocation after radiation exposure. Pasireotide did not protect the intestinal stem cells and the beneficial effect of Pasireotide could be reversed by pancreatic enzyme substitution. Therefore, Pasireotide does not seem to act as a cytoprotector, but to mitigate intestinal radiation injury by inhibiting pancreatic exocrine secretion.

Until recent, knowledge on the effects of Pasireotide on the radiation-induced tumor response was scarce or non-existing at all. Pre-clinical studies have shown that Pasireotide may have a direct inhibiting effect on the growth of certain tumors such as neuroendocrine cancers. Moreover, it may reduce tumor growth by reducing the availability of growth factors such as IGF-1 and VEGF. However, no studies have been performed to assess the effect of Pasireotide on radiation-induced tumor growth delay. As Pasireotide can only be considered for clinical use if it does not hamper the anti-tumor effect of radiotherapy, we tested the effect of Pasireotide on tumor response to radiation in an animal model. The results of this recently performed study may enable a trial to test the potential beneficial effect on intestinal radiation injury in patients.

SP-0031

Radiation induced proctopathy: lessons learned from prospective clinical trials

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The increasing number of dose escalation and hypofractionation prostate cancer trials is providing us excellent opportunities to learn more about ano-rectal,

bladder base and urethral radiation injuries. Our ability to predict these injuries prior to radiotherapy remains limited, however. For example, rectal dose volumes are a widely used planning tool, but published relationships between irradiated volumes and outcomes are inconsistent.
The presentation is a strictly clinical overview of the factors that contribute to ano-rectal radiation injuries and outlines recent progress in their management. Symptomatology resulting from rarely cited injuries, such as to the per-rectal fat and the pelvic floor musculature, are also discussed.

Symposium with Proffered Papers: Immobilisation, localisation and verification during image guided brachytherapy

SP-0032
Influence of immobilisation and implant stability during brachytherapy
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Abstract not received.

SP-0033
Role of target and applicator localisation under treatment delivery conditions
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Since the last 10 years 3D image-guided brachytherapy using CT, MRI, and/or ultrasound (US) has been introduced into clinical practice worldwide enabling conformation of the dose distribution to the target volume and avoidance of high dose to organs at risk (OAR). To be able to optimise the dose distribution in brachytherapy both the anatomy (target volume/OAR) *and* the applicator(s) should be correctly localised in the images. If the image modality does not enables both of these criteria the dose delivered the patient may be calculated incorrectly. Another important aspect is that the images should reflect the true situation at the time of the treatment. Due to the large dose gradient in brachytherapy, even small changes in the position of the applicator and/or anatomical structures may lead to discrepancies between planned and delivered dose. Usually, this is achieved with as short time as possible between imaging and treatment delivery.
The optimal image modality to use is depending on the site to be treated as well as the geometry and the material of the applicator. For cervical cancer MR imaging is the optimal modality to discriminate soft tissue and tumour. Concepts for image guided cervical brachytherapy have been developed by GEC-ESTRO and T2 weighted MR imaging is the preferred modality. In an interobserver study the mean inter-delineation distance of around 4 mm were found for the high risk CTV (HR CTV). The impact of these uncertainties for D90 and D100 (dose to 90% and 100% of the volume) were 10% and 19%, respectively.
Post-implant dosimetry after permanent prostate seed implantation is usually based on CT imaging. However, MR imaging has superior soft tissue contrast and is some times used nowadays. In an interobserver study the dosimetric consequence of the delineation uncertainty was estimated to be 18% for the prostate D90 when T2 and T1 weighted MR images were used. This figure was increased to 23% when the delineation was done on CT images.
Functional MR imaging, such as dynamic-enhanced MR, diffusion weighted imaging and MR spectroscopy, gives the opportunity to image microenvironmental characteristics of a tumour. Specific areas within the target volume with a high burden of disease or with biological characteristics indicating radioresistance may be targeted for higher dose delivery.
Even though MR imaging is excellent for target delineation, localisation of the applicators (i.e. the source path) or the seeds could be challenging. Some applicators (e.g. steel applicators or shielded applicators) are not even MR compatible. In general it is easier to visualise the applicator and source(s) in CT images. For rigid MR compatible applicators (e.g. plastic tandem-ring-applicator) so called library applicator files could be used. Then applicator file, including information about the applicator surface dimensions and the source path, can be imported into the MR images and rotated and translated until it matches the images. In some situations the needle tip could be difficult to localise in MR images. Then supplementary imaging could be used (e.g. CT) and image registration should be performed with the aim of matching the applicator geometry and not the bony anatomy. The dosimetric consequences of uncertainties in the applicator localisation are smaller compared to consequences of uncertainties in the target delineation. For the HR CTV D90 an average of 2% change per mm displacement of a ring applicator has been found in all directions.
Transrectal US (TRUS) is extensively used in prostate brachytherapy and gives an excellent view of the prostate gland. However, the presence of needles will preclude the image quality. Additionally, localisation of the needle tip could be challenging during needle reconstruction.
TRUS-based brachytherapy procedure offer a method for interactive treatment planning and, thus, short time between imaging and treatment delivery. Several groups have developed methods for “in treatment room” imaging with both CT and MR. However, for the latter method, challenges due to non MR compatible equipment is substantial.

SP-0034
Importance of treatment delivery verification
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Abstract not received.

OC-0035
Catheter displacement and dosimetry for single fraction MRI guided focal prostate HDR brachytherapy
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Purpose/Objective: The aim of this study is to analyze the effect of catheter displacement and anatomical variations (prostate and organs at risk) on the dose distribution in MRI guided single fraction high dose rate (HDR) focal brachytherapy of the prostate.
Materials and Methods: Twenty-two patients were treated with MRI guided focal HDR brachytherapy (Iridium-192) in a single fraction of 19 Gy. A multiparametric MRI was used to define the tumor region and was matched with the intraoperative ultrasound (US). For the treatment, self-anchoring umbrella catheters were used (1). For dose