studied, the mechanisms of its initiation and chronic extension still remain to be resolved. Yet, it is clear that development of fibrosis after radiation cannot simply be explained by the function of one molecule, but requires the interplay of several cytokines and growth factors and multiple cell types. Our studies have identified the TGF-β co-receptor endoglin as new player in radiation-induced fibrosis development in the kidney. Mice expressing halved levels of endoglin (Eng−/− mice) displayed reduced fibrosis but also less vascular damage after a single dose of kidney irradiation compared to irradiated Eng+/− mice. This was accompanied by decreased mRNA expression of Tgfβ1 and pro-fibrotic downstream targets such as Pai-1, Ctgf or Coi3A1. We also noticed that development of fibrosis in the kidney was accompanied by infiltration of inflammatory cells, mainly macrophages. Macrophages are crucial for tissue repair, but may also promote kidney fibrosis by secreting pro-fibrotic growth factors and cytokines as shown in several models of disease. Macrophage numbers were significantly upregulated in both irradiated Eng−/− and Eng+/− kidneys; however, the upregulation was less pronounced in Eng−/− mice. In addition, expression of macrophage-expressed pro-inflammatory, pro-fibrotic and anti-angiogenic cytokines interleukin 1-beta (Il1b) and interleukin 6 (Il6) was strongly reduced in the irradiated kidneys of Eng−/− compared to Eng+/− mice.

As endoglin is not only expressed on endothelial cells, but also on monocytes/macrophages, we are currently investigating whether changes in endothelial cell function or phenotype contributes to differential fibrosis formation in Eng−/− and Eng+/− mice. We are also analysing whether macrophage depletion prevents fibrosis formation after kidney irradiation. Furthermore, we are testing whether the anti-inflammatory, immunomodulatory and anti-fibrotic drug Thalidomide impedes the development of radiation-induced kidney fibrosis.

In summary, we suggest that endoglin mediates the inflammatory response in irradiated tissues by regulating macrophage infiltration and cytokine production thereby contributing to the development of irradiation-induced kidney fibrosis.

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**SYMPOSIUM: IMAGING FOR BRACHYTHERAPY**

**SP-0219**

**Imaging for brachytherapy: Head and neck, and prostate**

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Brachytherapy has benefitted considerably from advances in imaging techniques in recent times. Tumour volumetric-based radiation planning based on excellent delineation of tumour anatomy has much improved our ability to target malignant tissue whilst sparing non-malignant tissues. The highly conformal nature of Brachytherapy has further benefited from newer functional imaging techniques based on recognition of the altered biological and molecular processes occurring within tumour tissue. New paradigms for treatment planning and radiation delivery are now becoming possible based on the potential to define areas of varying functional activity within the anatomical tumour mass. Established 3D tumour volumes generated by morphological imaging techniques can now be modified by new information provided by functional imaging such as PET and MRI. Brachytherapy for prostate and Head & Neck cancers can benefit from data that quantifies areas of cellular and molecular disruptions within the tumour mass and thus offers the potential to individualise the Brachytherapy radiotherapy plan for each patient.

Prostate Brachytherapy includes both High Dose Rate and Low Dose Rate techniques and has become widely adopted as a valid treatment for prostate tumours. Historically, imaging has played a relatively small role in the management of clinically localized prostate cancer but in more recent years, medical imaging techniques, such as TRUS, CT and MRI have improved the clinical management of patients with prostate cancer. Brachytherapy offers the possibility of better local treatment with less morbidity and improved outcomes; more accurate imaging has contributed to better staging and patient selection as well as more accurately image-guided treatment delivery.

In the treatment of Head and neck tumours, Brachytherapy offers an excellent treatment for organ-preservation with local tumour control. Image guidance is central to the optimization of this treatment with careful dose escalation facilitated by accurate delineation of tumour and structures at risk. Adaptive image-guided Head & Neck Brachytherapy can complement newer surgical techniques and better understanding of tumour biology in this area will incorporate newer boost techniques also.

This inherent goal of Brachytherapy is to safely deliver adequate radiation to those areas of tumour tissue that are considered necessary based on our current understanding of tumour biology and radiation response. Imaging is central to the success of this treatment.

**SP-0220**

**Interstitial breast brachytherapy: the role of multimodality imaging**

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Before the era of breast conservation therapy using external beam radiotherapy (EBRT) and before the invention of linear accelerators and its widespread use in breast cancer treatment, brachytherapy using radium needles was the first method of breast irradiation. Interstitial breast implants started at the beginning of the XXth century either as mono-therapy or associated to surgery. Over the years, breast brachytherapy was less and less used but it remained an option as a boost to EBRT. Nowadays with the increase use of partial breast irradiation, breast brachytherapy is gaining more importance. Unlike prostate, breast brachytherapy is not widely practiced because it was always considered by many to be too operator- and skill-dependent, partly because of the lack of easy and precise imaging. It is evident that for more accuracy, imaging is necessary in breast brachytherapy as it is in EBRT, to plan and optimize the treatment. The need of accuracy is even more important in brachytherapy because it provides the most conformal coverage of tumor and normal tissue sparing radiotherapy technique.

In this era of highly targeted radiotherapy, breast brachytherapy faces the same challenges of volume delineation at each step of the process: in pre-planning, during implant and at dosimetry. The first step is the identification of the surgical bed to be implanted. This is not an easy task as reflected by the numerous papers in the literature. At the time of brachytherapy the cavity is often collapsed and difficult to find. We conducted a phase II study Using MRI imaging to help in the delineation of the surgical bed and therefore help to plan precisely where to place the implant. The second step is the precise placement of the interstitial needles into the breast around the target. This is of great importance since it will, in a way, determine the dosimetry. Ultrasound can be used as a step-by-step procedure. As in prostate brachytherapy a real-time imaging during the procedure would be ideal. The ultimate step, the dosimetry, is to maximize the dose to the target volumes and to minimize the dose to the adjacent organs at risk. At this step the quality of imaging is important for the delineation of the volumes and for reconstruction of the material implanted. CT scan allows implant reconstruction very easily but MRI allows accurate surgical bed delineation. Therefore a robust image fusion capacity has to be available. Ultimately, the goal would be to find a 3D imaging modality that could serve both purposes and could be integrated in the treatment planning system.

This presentation is aimed to determine the role of modern imaging modalities in all the steps of interstitial breast brachytherapy. It is our opinion that more accurate imaging will help the wide application of interstitial brachytherapy for breast cavity boost, partial breast irradiation and second conservative treatment for in-breast recurrences.

**SP-0221**

**Gynaecology**

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Abstract not received

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**SYMPOSIUM: EU PROJECTS 2**

**SP-0222**

**First clinical experience with head and neck and lung cancer patients within the ARTFORCE project**

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The ARTFORCE project (Adaptive and innovative Radiation Treatment FOR improving Cancer patients treatment outcome) that now runs for more than a year, consists of two clinical trials, combined with fundamental research in molecular biology, i.e. predicting tumour response and physics: image guidance and dosimetry performed in a multi-institutional environment.

The non-small cell lung cancer study aims to improve local control and test the hypothesis of iso-toxic dose redistribution. Patients are...