**SP-0046 Avoiding side effects: getting the best out of advanced delivery techniques**

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**Abstract text**

Several systematic factors influence the dose to the heart and lungs in breast cancer radiotherapy. In this presentation, we will review the dosimetric benefits of alternative positioning (prone and lateral decubitus) and different delivery techniques (VMAT, hybrid VMAT, simultaneous integrated boost) when different nodal regions are included in the target volume. The role of image guidance strategies and their potential to reduce uncertainties will also be discussed.

**SP-0047 Between high-tech and biology: how to exploit protons, minibeams and flash irradiation to avoid toxicity?**

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**Abstract text**

Numerous data are available supporting the evidence of the benefits of radiotherapy in the treatment of breast cancer, that include a high rate of local control following either breast-conserving surgery or mastectomy and its contribution to significantly reduce long term metastasis and death rate. Radiotherapy has allowed women with early stages to preserve their breast with excellent cosmetic results and limited long term sequelae. However, acute and long-term toxicities remain an issue, especially since overall survival is increasing in patients with breast cancer. Treatment-related toxicities include breast deformation and fibrosis, skin changes, pain, cardiac and pulmonary morbidities, brachial plexopathy, and radiation-induced malignancies. This review will focus on new innovative radiation therapy technologies, and how they could potentially be used in the future to increase further the differential effects of radiotherapy in breast cancer

**Proton therapy**: Though proton therapy (PT) was used for almost 30 years to treat patients with cancers of the eye, base of skull, vertebral axis, and children, only recently has it been tested in other cancer locations such as breast cancer. These extensions were made possible by the development of new techniques such as on-board imaging and pencil beam scanning (PBS). Because of the specific physical properties of a proton beam (the Bragg peak and reduced penumbra among others), PT could significantly reduce cardiac, neurologic and contralateral breast toxicity in some patients receiving lymph nodes irradiation. Small retrospective series1-4 demonstrated the feasibility of treating the breast or chest wall and lymph nodes areas with acceptable acute toxicity. Prospective randomized trials are under development in Europe and the USA. In addition to its physical properties, biological specific properties of PT on induction of DNA-damage, its role in inflammation and potential immune modulation, as well as the variations of its relative biological equivalence (RBE) along its path in the tissues and in the Bragg peak could represent interesting properties to use in in subgroups of patients with aggressive breast cancer.

**Minibeam radiotherapy**: Minibeam radiotherapy (MBRT) is a technique that was tested in preclinical animal models only. It aims at creating spatial dose fractionation using infra-millimetric field sizes with an array of thin, parallels beams. Dose is distributed along "valleys" and "peaks" and it has been shown to significantly increase the tolerance of normal tissues in animal models[5]. This technology is currently under development using protons minibeam (pMBRT), taking advantage of the ballistic and biologic properties of proton irradiation[6]

Biological properties of ultrahigh rate irradiation: the FLASH irradiation effect: FLASH radiotherapy delivers high irradiation doses at ultrahigh rates, within milliseconds. In mice models receiving high single irradiation doses of 17 to 30 Gy, it has been shown to spare normal tissues (lungs, skin, brain, bone marrow) while preserving the radiation effect on tumours, compared to conventional rate irradiation[7]. The biological mechanisms involved in this highly differential effect are not completely elucidated, and may involve, among others, the sparing of DNA repair capacity of quiescent normal tissue cells, and epithelial cells protection from radiation induced apoptosis. Specifically designed accelerators were used in these experiments, using low energy electrons at dose rates over 50 Gy/s (> 3000 Gy/mn), at least 2000 times higher than the highest available clinical dose rate on conventional linear accelerators While the technology to build high energy linear accelerators that could be used to treat patients with photons at such high rates does not exist, proton therapy cyclotrons can attain this ultrahigh dose rate within the pencil beam. Technological developments and experiments on animal models are on-going using FLASH irradiation with proton.

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**SP-0048 Second cancers after radiotherapy for breast cancer**

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**Abstract text**

Introduction: For more than 50 years radiotherapy has played an essential role in the treatment of primary loco-regional breast cancer, as it has been shown to improve both loco-regional tumour control as well as overall survival, by a few percent, in suitable women. Additionally, radiotherapy is increasingly being used after DCIS (ductal carcinoma in situ), as trials have shown that radiotherapy halves the risk of ipsilateral invasive disease, but with no apparent effect on the 10 year breast cancer-specific mortality. Cure however, has come at a price, as radiotherapy can induce second cancers decades after the initial treatment. Results: A review of the excising litterateur, have quit consistently shown, that radiotherapy after breast cancer can induce second solid cancers, that primarily are located in close proximity to the former treatment fields. Thus in a large meta-analysis including approximately 700.000 breast cancer patients, radiotherapy was associated with an increased risk of second lung; RR 1.66 (95% CI 1.36-2.01) and oesophagus cancers RR 2.17 (95% CI 1.11-4.25) +15 years after treatment, as well as second sarcomas (+5 years after treatment) RR 2.53 (1.74-3.70). Similarly, in another meta-analysis that included over 500.000 breast cancer patients, irradiated patients had an increased risk of second lung RR 1.91 (95% CI 1.11-3.29), esophagus RR 2.71 (95% CI 1.96-3.76) and thyroid cancer RR 3.15 (95% CI 1.34-7.42) as well as second sarcomas RR 6.54 (95% CI 3.54-12.10) +10 to +15 years after treatment, compared to the general female population. For non-irradiated