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**Purpose:** Carcinoma-Associated Fibroblasts (CAFs) are major components of solid malignancies and play central roles in cancer sustainability. In this study we have investigated the invasive capacity and matrix remodelling properties of human lung CAFs after exposure to ablative doses of ionizing radiation (IR), corresponding to fractions delivered by stereotactic ablative radiotherapy (SART) for medically inoperable stage-I/II non-small-cell lung cancers.

**Methods:** CAFs were isolated from lung tumor specimens from 15 donors. The migrative and invasive capacities of CAFs were determined after a sub-lethal single radiation dose of 18 Gy. To ascertain the mechanisms behind the altered invasive capacity of cells, the expression of matrix metalloproteinases (MMPs) and their endogenous inhibitors (TIMPs) were measured in the conditioned media several days post-irradiation, along with the expression of cell surface integrins and the dynamics of focal contacts by vinculin-staining.

**Results:** Exposure to 1x18 Gy resulted in premature cellular senescence and caused inhibition of the proliferative, migrative and invasive capacity in CAFs. IR promoted MMP-3 and inhibited MMP-1 appearance to some extent, but did not affect the expression of other major MMPs. Furthermore, surface expression of integrins  $\alpha 2$ ,  $\beta 1$  and  $\alpha 5$  was consistently enhanced, and a dramatic augmentation and redistribution of focal contacts was observed.

**Conclusions:** Our data indicate that ablative doses of IR, which are increasingly offered by hypofractionated radiotherapy regimens, exert advantageous inhibitory effects on the proliferative, migratory and invasive capacity of lung CAFs. The reduced motility of irradiated CAFs might be a consequence of partial reduction in MMP-1 expression and stabilization of focal contacts via integrins.

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#### DEVELOPING COMPUTATIONAL METHODS TO VIEW DISTRIBUTIONS OF SECOND CANCER RISK USING MONTE CARLO AND VOXEL HUMAN PHANTOMS

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**Objectives:** Radiotherapy has developed greatly in the last 30 years. Many advanced techniques have emerged in the clinical practice, having promising goals to cure cancer with less treatment side-effects to patients. However, with increasing longer survival, concerns about radiation-induced second cancers have increased. New techniques such as Intensity Modulated Radiation Therapy IMRT and proton therapy have changed the simple uniform dose distribution received by the patient to more escalated and complex radiation fields, which are not easy to estimate with traditional methods. The need for an accurate tool to calculate dose distributions for normal tissue has become an important issue. Additionally CT data for the whole

body is generally not available for calculating dose to distal organs. Voxel human phantoms, which offer a idealised human representation are construct from CT and MRI images, are combined with calculations of the dose using the Monte Carlo method to calculate very precise estimates of dose distributions and risk.

**Methodology:** Radiotherapy prostate plans have been simulated using the reference male voxel phantom, which developed by ICRU, using the EGSnrc user code DOSXYZnrc for modelling the phantom and verification of a 10MV X-ray beam from an head model of the Elekta Precise linear accelerator which is modelled using BEAMnrc. Detailed information about out of field radiation, including external charged particle production, will be studied. Results will be linked to second cancer rates and distributions reported in epidemiological studies.

**Results and Conclusion:** Development for accurate tools to estimates and visualise the distributions of risk for different radiation modalities has become an argent need, in order to cope with the rapid changes in the radiotherapy plus the increase in the survival rate after radiotherapy. Monte Carlo can simulate a wide range of radiation energies and particles, including contaminant electrons and neutrons. Monte Carlo calculation time can be minimised using cluster computers. While the human voxel phantom is fixed in its orientation, the development of methods to the change of size, age, and radiotherapy orientation is also of strong interest.

#### References

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#### LONG-TERM RESULTS AFTER HDR 252-CF BRACHY THERAPY AND EBRT FOR CA CERVICIS UTERI

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In the period November 1996-March 1998 92 pts with Ca cervicis uteri(2B-28 pts and 3B-64 pts) received combined RT(HDR <sup>252</sup>Cf neutron brachytherapy and EBRT)

**Materials and methods** All pts received median total dose to the point A 77 Gy(50-79) and to the point B 60 Gy(39-65).The total dose including median total EBRT dose(point A-37 Gy,point B-50 Gy) and five brachytherapy sessions 1.4 neutron+0.9 gamma Gy to the point A each. According Rjabuchin formulae the brachytherapy dose respond to 8 isoGy.

**Results** The overall survival rate at 5,10 and 15 yr for stage 2B was 67.9%, 60.7% and 50.8%,for stage 3B 48.4%,42.2% and 40.6% respectively. 5(5.4%) late complications (grade 2 and 3),11(12%recurrences, 5(5.4%)distant metastases and 3(3.3%) second primaries were observed. The impact and correlation of different parameters on the overall survival should be presented.