| | |
|---|---|
| **Titre:** Title: | 78: Development of a trap to attract and eliminate cancer cells infiltrated into the brain |
| **Auteurs:** Authors: | Angela Giraldo, Nathalie Faucheux, Nick Virgilio, Marc-Antoine Lauzon, Suzanne Gascon, Hélène Therriault, & Benoit Paquette |
| **Date:** | 2020 |
| **Type:** | Communication de conférence / Conference or Workshop Item |
| **Référence:** Citation: | Giraldo, A., Faucheux, N., Virgilio, N., Lauzon, M.-A., Gascon, S., Therriault, H., & Paquette, B. (septembre 2020). 78: Development of a trap to attract and eliminate cancer cells infiltrated into the brain [Résumé]. CARO Virtual Scientific Meeting in partnership with the CAMRT "Equity in Radiation Oncology: Patients Providers and Practice". Publié dans Radiotherapy and Oncology, 150. https://doi.org/10.1016/s0167-8140%2820%2930970-1 |



| | |
|---|---|
| **Nom de la conférence:** Conference Name: | CARO Virtual Scientific Meeting in partnership with the CAMRT "Equity in Radiation Oncology: Patients Providers and Practice" |
| **Date et lieu:** Date and Location: | 2020-09-23 - 2020-09-25 |
| **Maison d'édition:** Publisher: | Elsevier |
| **URL officiel:** Official URL: | https://doi.org/10.1016/s0167-8140%2820%2930970-1 |
| **Mention légale:** Legal notice: | |

heart, spinal cord, liver and kidneys must be considered. Low dose spread is of particular concern with respect to healthy lung tissue. This study comprehensively compares volumetric dose statistics of the standard CRT compared with VMAT and IMRT for esophageal cancer treatment.

**Materials and Methods:** Forty patients who underwent pre-operative radiation therapy for esophageal cancer between 2012-2014 were retrieved from our database. Pinnacle Planning Software was used to create CRT, VMAT and IMRT radiation plans for all patients. 45Gy was prescribed for each patient with $D_{95\%}$ > 42.75Gy for the planning target volume (PTV). All plans were optimized to maintain PTV coverage while reducing dose to OAR with specific emphasis on lung and heart dose. Volumetric dose statistics were obtained and Wilcoxon signed rank test was used to compare CRT versus IMRT and VMAT for Lung ($V_{5Gy}$, $V_{20Gy}$, mean, max), Heart ($V_{30Gy}$, mean, max), Spinal Cord max, Bilateral Kidneys ($V_{20Gy}$, mean) and Liver mean dose.

**Results:** For both IMRT and VMAT compared with CRT, statistically significant differences were noted for Lung ($V_{20Gy}$ -49.7%,-57.4%, Mean -20.3%,-24.9%, p<0.001), Heart ($V_{30Gy}$ -10.1%,-16.7%, Mean -10.4%,-13.4%, p<0.001). Kidneys ($V_{20Gy}$ -60.4%,-55.2%, p<0.001), spinal cord (Max 6.8%,6.0%, p<0.01- IMRT; p<0.003-VMAT) and Liver (Mean -29.9%,-24.3%, p<0.001). No statistically significant differences were noted for VMAT and IMRT compared with CRT for Lung ($V_{5Gy}$, max dose), Heart (max; IMRT only) and Bilateral Kidneys (mean).

**Conclusions:** VMAT and IMRT offer excellent sparing of key organs (lung, heart) with respect to volumetric constraints. Max point doses as well as Lung $V_{5Gy}$, which can be an indication of low dose spread for esophageal treatment, were not conclusively different. While CRT offers acceptable treatment, VMAT and IMRT should be the standard modality of radiation treatment where facilities exist.

**78**

## DEVELOPMENT OF A TRAP TO ATTRACT AND ELIMINATE CANCER CELLS INFILTRATED INTO THE BRAIN

Angela Giraldo[1], Nathalie Faucheux[1], Nick Virgilio[2], Marc-Antoine Lauzon[1], Suzanne Gascon[1], Hélène Therriault[1], Benoit Paquette[1]
[1]*Université de Sherbrooke, Sherbrooke, QC*
[2]*École Polytechnique de Montréal, Montréal, QC*

Glioblastoma cells (GBM) that leave the tumour and then infiltrate into the brain are the main cause of treatment failure. Our overall aim is to improve the ability of radiation to eliminate these GBM cells, while preserving healthy brain tissue. To achieve this goal, we are developing a macroporous matrix which, using the chemoattractant CXCL12, will attract the GBM cells. Once trapped, the GBM cells will then be safely irradiated by stereotaxic radiosurgery. The first version of the matrix was made with alginate. This matrix has fully interconnected pores with an average diameter of 200µm and was functionalized with the cell-adhesion peptide RGD (CGGRGDS) at a density of 3.5 x $10^{-7}$ mol/400mg alginate. The GBM cells U87 (human) and F98 (rat) successfully accumulated and adhered on the surface of matrix pores. The chemoattactant CXCL12 was encapsulated into nanoparticles (CXCL12-NPs) made of alginate/chitosan in order to control its release rate. This encapsulation didn't affect its activity, as assessed with an in vitro invasion assay. The 3D migration system will be used to determine the quantity of the CXCL12-NPs to load in the matrices that will allow the migration of GBM cells over a distance of 2mm and 2cm, which are respectively required for the animal model and the human brain. The in vitro results also demonstrate that the F98 cells accumulated into the matrix can be eliminated with a radiation dose of 25Gy.

**79**

## MULTI-PARAMETRIC MAGNETIC RESONANCE IMAGING OF MULTI-FOCAL PROSTATE CANCER UNMASKS INTRA-PROSTATIC GENOMIC HETEROGENEITY AND NOVEL RADIO-GENOMIC CORRELATES: RESULTS OF THE SMARTER PROSTATE INTERVENTIONS AND THERAPEUTICS (SPIRIT) STUDY

Rohann J. M. Correa[1], Erfan Aref-Eshghi[1], Ryan Alfano[1], Bekim Sadikovic[1], Aaron D. Ward[1], Paul C. Boutros[2], John M. S. Bartlett[3], Zahra Kassam[1], Joseph L. Chin[1], Stephen E. Pautler[1], Mena Gaed[1], José A. Gómez[1], Madeleine Moussa[1], Glenn S. Bauman[1]
[1]*Western University, London, ON*
[2]*University of California, Los Angeles, CA*
[3]*University of Toronto, Toronto, ON*

**Purpose:** Multi-focality and heterogeneity in prostate cancer can confound the selection of appropriate clinical management. Our study aimed to explore radio-genomic correlations using multiparametric magnetic resonance imaging (mpMRI) against a histopathologic reference standard.

**Materials and Methods:** Eligible men with prostate cancer underwent mpMRI followed by prostatectomy. Whole-mount histopathology was digitized and co-registered to corresponding MRI slices using high-fidelity methodology validated at our institution. (1) Foci, including central/transitional and peripheral zone lesions, were identified by a pathologist then macrodissected for genomic copy-number aberration (CNA) analysis.

**Results:** We found a broad range of CNAs revealing inter-patient and intra-prostatic heterogeneity. Only radiomic features derived from apparent diffusion coefficient (ADC) independently correlated with both Gleason grade (Rho=-0.62, p=0.003) and median CNA burden (Rho=-0.68, p<0.001). While greater CNA burden expectedly correlated with higher grade, intermediate-grade (Gleason score 3+4 or 4+3) lesions appeared more like either high-grade (Gleason scores ≥4+4) or low-grade (Gleason score 3+3) disease when clustered based on CNA and ADC metrics.

**Conclusions:** These findings suggest ADC-derived radiomic metrics may be a useful imaging biomarker across both central and peripheral zone lesions and could aid in further characterization of intra-prostatic biologic heterogeneity. These proof-of-principle data reveal novel radio-genomic correlations that could supplement histologic grading and conventional imaging. Validation studies are now underway in an expansion cohort of approximately eight additional men (24 tumour foci) and updated analyses of CNA and whole-genome methylation will be presented.

1. Ward et al. Radiology 2012; 263(3):856-64.

**80**

## SPIRONOLACTONE EXPOSURE IS ASSOCIATED WITH REDUCED INCIDENCE OF PROSTATE CANCER: A POPULATION-BASED PHARMACOEPIDEMIOLOGIC STUDY

Bryan Janzen, Brett Hiebert, Rohan Sanjanwala, Aldrich Ong, Julian Kim, Ross Feldman
*University of Manitoba, Winnipeg, MB*

**Purpose:** Aldosterone is a potent agonist of the G-Protein coupled Estrogen Receptor (GPER), which in turn has stimulatory effects on prostate cancer growth in cell cultures and murine models. Spironolactone, an antimineralocorticoid used for management of congestive heart failure (CHF) is an antagonist of GPER with known antiandrogenic effects. This study aimed to determine if spironolactone exposure amongst men with CHF was associated with reduced prostate cancer incidence.