assurance, to limit the required resources, and to reduce the effect of differences in patient positioning between the planning CT and treatment. The patient is treated both prone and supine under a 1 cm clear plastic sheet positioned 20 cm from their surface used to increase skin dose. The first patient treated using this technique at the TBCC was a 16-year-old male with sickle-cell anemia. As gonadal shielding was desirable for this patient, our extended SSD lateral field technique was not an option. Our optimized VMAT technique allowed us to provide a reasonable amount of gonadal shielding using MLCs.

**Results:** Dose to the gonads was further reduced using a physical shield made of coated lead positioned above the gonads using an in-house designed device. The combined effect of these two types of shielding allowed us to reduce dose to testis from the prescription of 20 GY to approximately 100 cGy, without compromising dose uniformity to the rest of the body.

**Conclusions:** In conclusion, a new TBI technique has been developed using VMAT delivery that is optimized to patient anatomy. In addition to a safe and more comfortable patient environment, this technique allows for shielding of organs at risk, if desired by the physician, as was the case for a recent patient at the TBCC – a pediatric sickle-cell anemia patient requiring scrotal shielding.

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**COMBINED SALICYLATE (SAL) + METFORMIN (MET) TREATMENT INDUCES INCREASED TUMOUR SUPPRESSION AND RADIO-SENSITIZATION IN PRECLINICAL MODELS OF PROSTATE CANCER (PrCa).**

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**Purpose:** Tumour metabolism is a promising area of cancer research which is investigated to develop strategies for PrCa prevention and sensitization to cytotoxic therapy. AMP-kinase (AMPK) is a master regulator of cellular metabolism and a well-studied target for metabolism modulating therapeutics. It inhibits energy expenditure through anabolic events and stimulates substrate uptake and catabolic activities to increase energy availability. We showed that AMPK also senses genotoxic stress. It is activated downstream of Ataxia Telangiectasia Mutated (ATM) and leads to i) induction of p53 and cyclin-dependent kinase inhibitors p21cip1/p27kip1 and inhibition of cell cycle and proliferation and ii) blockade of protein biosynthesis and survival through inhibition of the AKT–mTOR pathway.

We found the anti-diabetic biguanide metformin (MET) and the metabolite of aspirin Salicylate (SAL) activate AMPK through separate mechanisms and suppress de novo lipogenesis, which is required for cellular growth and cell division. Combined treatment with SAL + MET enhanced AMPK activity, suppressed lipogenesis and inhibited PrCa proliferation and clonogenic survival significantly more than each agent alone. Interestingly, retrospective studies link MET and aspirin with improved responses to RT.

**Methods and Materials:** Androgen sensitive (22RV1) and and insensitive (PC3) PrCa cells were treated with SAL, MET and SAL + MET without or with increasing doses of radiotherapy (RT) (0–8 Gy) and were subjected to proliferation, clonogenic survival and immunoblotting (IB) experiments. Also, cells were grafted into flanks of immunosuppressed nude mice, treated with SAL, MET and SAL + MET and were subjected to proliferation, clonogenic survival and immunoblotting (IB) experiments. We showed that MET and aspirin sensitized PrCa cells to RT and increase activation of the ATM-AMPK pathway. Importantly, the combined SAL + MET treatment enhanced significantly the sensitivity of PrCa cells to RT compared to each agent alone. Ongoing experiments evaluate the effects of combined SAL + MET treatment on tumour growth kinetics.

**Conclusions:** Early results on the investigation of combined SAL + MET treatment indicate that this may be a promising therapy against PrCa tumour growth and radio-resistance. The two agents are extensively-used, well-tolerated and economical therapeutics and there are no reports associating them with increase RT toxicity. If positive, our studies will generate the first basis for future rapid clinical investigation of combined SAL + MET with RT in PrCa.

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**STEREOTACTIC BODY RADIOTHERAPY FOR METASTATIC NON-SMALL CELL LUNG CANCER: OLIGOMETASTASES, OLIGOPROGRESSION, AND LOCAL CONTROL.**

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**Purpose:** Use of SBRT to treat metastatic tumours is increasing, despite no randomized evidence. This project reviews the outcomes of treating extracranial NSCLC metastases with SBRT from a single institution.

**Methods and Materials:** One hundred and eight patients with metastatic NSCLC were treated between 2009 and 2015. Indications for treatment were: 1) oligometastases, where the goal was to irradiate all tumour sites; 2) oligoprogression, where the goal was to irradiate only tumours which were progressing while all other tumours were stable on observation or systemic therapy; and 3) for dominant tumours, where the goal was to optimize local control, even if other tumours were progressing. Outcomes of interest were local control (LC), overall survival (OS), progression-free survival (PFS), and time to change systemic therapy (TT CST).

**Results:** Median age was 69.0 years. Median follow up time was 11.3 months. Sixty-six patients were treated for oligometastases, 20 for oligoprogression, and 22 for dominant tumour/local control. Thirteen patients had targeted oral therapy, and 51 had chemotherapy prior to SBRT. Eleven were on systemic therapy (four targeted oral therapy and seven chemotherapy) at time of SBRT and a total of 165 lesions were treated (44 lung, 60 spine, 27 non-spine bone, 15 liver, 15 adrenal, 4 other sites). Median SBRT dose/fractions was 35 Gy/4 fractions. Median BED10 was 59.5 Gy, although 61 lesions (37%) were treated with BED10 of ≥ 100 Gy. LC at one year and two years was 80.2% and 64.4%, respectively. Univariate analyses revealed BED10 ≥ 100 Gy (p = 0.0142), tumour size ≤ 4 cm (p = 0.0012), and lung tumour (p = 0.0421) to predict for higher LC. Two year LC was 90.3% versus 52.1% for tumours treated with BED10 ≥ 100 Gy versus < 100 Gy. Median OS was 27.3 months. Indication for treatment independently predicted for OS (p = 0.0045) with oligometastases patients living the longest, followed by oligoprogression, and then dominant tumour/local control (median OS of 39.3 months, 21.1 months, and 11.8 months, respectively). Median PFS was 4.4 months, with indication for therapy; and 3) for dominant tumours, where the goal was to optimize local control, even if other tumours were progressing.

**Conclusions:** Small Cell Lung Cancer: Oligometastases, Oligoprogression, and Local Control.