9th Annual Scientific Meeting - The Next Generation

3rd June 2021 Half Day Virtual Meeting

Via Platform

Abstracts

Committee Members:

Anthony Chalmers (Chair)
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Aileen Duffton
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Claire Paterson
Lesley Samuel
Sean O'Cathail

Half Day Programme
The Next Generation
Thursday 3rd June 2021

12.30	Welcome & Introduction	*Anthony Chalmers, Glasgow*

Chair ***Bill Nailon, Edinburgh***

Optimising Outcomes for Patients with Pelvic Malignancies

12.40	Optimising Radiotherapy for Rectal Cancer (12 + 3 mins)	*Sean O'Cathail, Glasgow*
12.55	The Impact of MRI in Radiotherapy Treatment Planning for Rectal Cancer (10 + 2 mins)	*Lynsey Devlin, Glasgow*
13.07	Real-Time Tracking for Dose Escalated Prostate SBRT (10 + 2 mins)	*Michael Trainer, Edinburgh*
13.19	The SCOT Trial – was it worth it? Assessing the Impact of Cancer Clinical Trials (10 + 2 mins)	*Catherine Hanna, Glasgow*
13.31	Impact of Treatment Delivery Time on Rectal Volume and Toxicity during SABR Prostate Therapy (10 + 2 mins)	*Joanne Mitchell, Edinburgh*

13.40 – 14.00 BREAK

Chair ***Stephen Harrow, Edinburgh***

Optimising Radiotherapy for Lung Cancer Patients

14.00	Improving Patient Fitness for Lung Cancer Treatment (12 + 3 mins)	*Iain Phillips, Edinburgh*
14.15	Overview of PhD Findings – Overcoming Hypoxia in Lung Cancer (12 + 3 mins)	*Kirsten Laws, Aberdeen*
14.30	Overview of PhD Findings – Re-Irradiation for Lung Cancer (12 + 3 mins)	*Rob Rulach, Glasgow*
14.45	Cell-free and circulating tumour DNA as a biomarker in patients receiving stereotactic ablative radiotherapy for early-stage lung cancer (12 + 3 mins)	*Angus Killean, Edinburgh*

15.00 – 15.15 TEA BREAK

Chair	***Kirsten Laws, Aberdeen***	
15.15	**Proffered Papers – Four Oral Presentations (each 8 + 2 mins)**	
	- Kirsty Nash - Mark Jackson - Lisa Hay - Cicely Cunningham	
	15.55 – 16.10 BREAK	
16.10	**Optimising Radiotherapy for Head & Neck and Brain Cancer Patients**	
16.25	Radiomics/Head and Neck Cancer (12 + 3 mins)	*David Noble, Edinburgh*
16.40	Radiotherapy Dose Escalation for Patients with High Risk Oropharyngeal Squamous Cell Cancers (MERINO-2) (12 + 3 mins)	*Laura Grocutt, Glasgow*
16.55	Hippocampal Sparing for Low Grade Glioma (12 + 3 mins)	*Aoife Williamson, Glasgow*
	Closing Remarks	*Anthony Chalmers, Glasgow*

Session 1 – Optimising Outcomes for Patients with Pelvic Malignancies

Optimising Radiotherapy for Rectal Cancer

Sean O'Cathail

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Bowel cancer is the 4th most common cancer type and rectal is the most frequent location. Recent important phase 3 clinical trial data have expanded the evidence base for multimodal treatment and increased the available clinically relevant options for patients. But important questions remain about the biological underpinnings of individual level responses to radiation. There are no available biomarkers of radiation response/resistance.

Current multidisciplinary collaborations in Glasgow are focussed on shedding light on the nature of tumour microenvironment responses and exploring novel aspects of cancer associated metabolism. Coupled with an expanding program of early phase, translationally rich clinical trials we aim to optimise the use of neoadjuvant rectal cancer strategies, to address patient orientated questions such as de-escalation and biomarkers of resistance to include patients in treatment intensification strategies.

The Impact of MRI in the Radiotherapy Planning of Rectal Cancer

Lynsey Devlin

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All radiotherapy (RT) indications for locally advanced rectal cancer (LARC) are defined by clinic-radiological magnetic resonance imaging (MRI) defined criteria. Accurate and precise delineation of the target volume is fundamental to the success of RT.

CT planning scans can have poor soft tissue contrast and target delineation on this dataset can overestimate tumour volumes. Given that MRI brings superior visualisation of soft tissue in the diagnostic phase of LARC, there is a move towards routine use of MRI within the delivery of radiotherapy. MRI is long recognised as the gold standard in the staging and response assessment of rectal cancers. The rectum lends well to the exquisite soft tissue definition MRI offers, and additional functional information can be used to further characterise tumour.

Improved tumour localisation up front and assessment of responses during radiation has the potential to improve patient outcomes in numerous ways. With growing evidence to support a dose response relationship for rectal cancer and the future potential of functional sequences to assist planning of boost regimes. This technology brings the capability of real time adaption, to change the plan based on anatomical and functional imaging.

The ability to acquire serial imaging during radiotherapy, incorporate this information back to tumour assessment and ultimately response is potentially paradigm changing. Although there is a general acceptance that the use of MRI in rectal cancer radiotherapy planning is superior, the correct application of MRI in RT planning is crucial to ensure the optimal benefit is gained.

Real-Time Tracking for Dose Escalated Prostate SBRT

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Aim

To investigate the use of the RayPilot tracking system to help treat prostate SBRT with a dose escalated boost.

Method and materials

Seven patients in the PRINToUT trial received prostate SBRT (36.25Gy in 5#) treated using 3 VMAT arcs delivered on Truebeam linacs and planned using the Eclipse TPS (v13.6). Pre-treatment imaging was with kV orthogonal and CBCT and tumour tracking using the RayPilot system. RayPilot uses an electromagnetic transmitter inserted into the prostate. The position of the transmitter was analysed retrospectively using the RayPilot system readout and the transmitter position on CBCT images. A planning study, adding a dose escalated boost to the prostate SBRT plans was carried out, with additional plans simulating degrees of patient displacement from the clinical imaging data. All new plans were assessed against the PRINToUT protocol.

Results

From the CBCT images, the mean displacement of the RayPilot transmitter comparing the CT and the CBCT scans was -0.04cm(x), 0.07cm(y) & 0.16cm(z). The RayPilot system recorded all treatments except #3, 4 & 5 for patient 4 due to technical issues with the mean displacement of the transmitter within 003cm. In the planning study the PTV, CTV and PTV(boost) dose coverage was acceptable with dose escalation but only two patients in the study met all of the rectum dose constraints. Simulating the CBCT positional data, PTV coverage was not met on four patients and for the RayPilot data the plan dosimetry was not significantly affected by the displacements.

Conclusion

The RayPilot tracking system could be used in the treatment of prostate SBRT with a dose escalated boost. Further studies would be required before this could be used as a primary imaging method for patient positioning.

The SCOT Trial – was it worth it? Assessing the Impact of Cancer Clinical Trials

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Introduction

Cancer clinical trials, whether investigating radiotherapy, systemic anti-cancer therapies or combination treatments, require major investment, monetary and otherwise. With increasing competition for the charity pound due to Covid-19, selecting which research to support is an important consideration for funders, pharmaceutical companies and Clinical Trials Units. Assessment of the wider impact of cancer trials can support this allocation of resources, as well as showing accountability for investment, demonstrating how impact occurs and advocating for future research funds. This study investigated how the impact of a cancer trial can be evaluated.

Methods

The wider impacts resulting from investing in the Short Course Oncology Treatment (SCOT) trial were evaluated by calculating the direct healthcare service savings, as well as the potential QALY gain, from implementation of trial findings. An international survey and national level, real world data were used to estimate the extent of implementation. Cost and QALY gains were estimated using a cost-utility analysis (CUA) and applied within a budget impact analysis to estimate the economic value of the SCOT trial investment.

Results

There was a high level of practice change in line with SCOT trial results, with chemotherapy regimen and disease stage shown to be important determinants of practice. Cost estimates applied to this practice change showed that the value of implementing SCOT amounted to over $150 million USD over 5 years from the perspective of all countries that recruited to SCOT. Adopting a societal perspective by considering travel costs and work related productivity loss increased this estimate $340 million USD. QALY gain from implementation was calculated at $116 million USD over 5 years. The estimated investment to perform the SCOT trial was $8.8 million USD.

Discussion

Research impact evaluation can be applied to cancer trials to demonstrate the value of cancer research investment and to advocate for ongoing funding in a time of increasing austerity. The methods used in this study could equally be applied to radiotherapy trials in future.

Impact of Treatment Delivery Time on Rectal Volume and Toxicity during SABR Prostate Therapy

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Keywords: Prostate , SABR, treatment time, toxicity , hypofractionation .

Objectives

The aim of this study was to investigate any relationship between patient reported gastrointestinal toxicity scores and the time it takes to deliver individual radiotherapy fractions during a course of prostate stereotactic radiotherapy (SBRT).

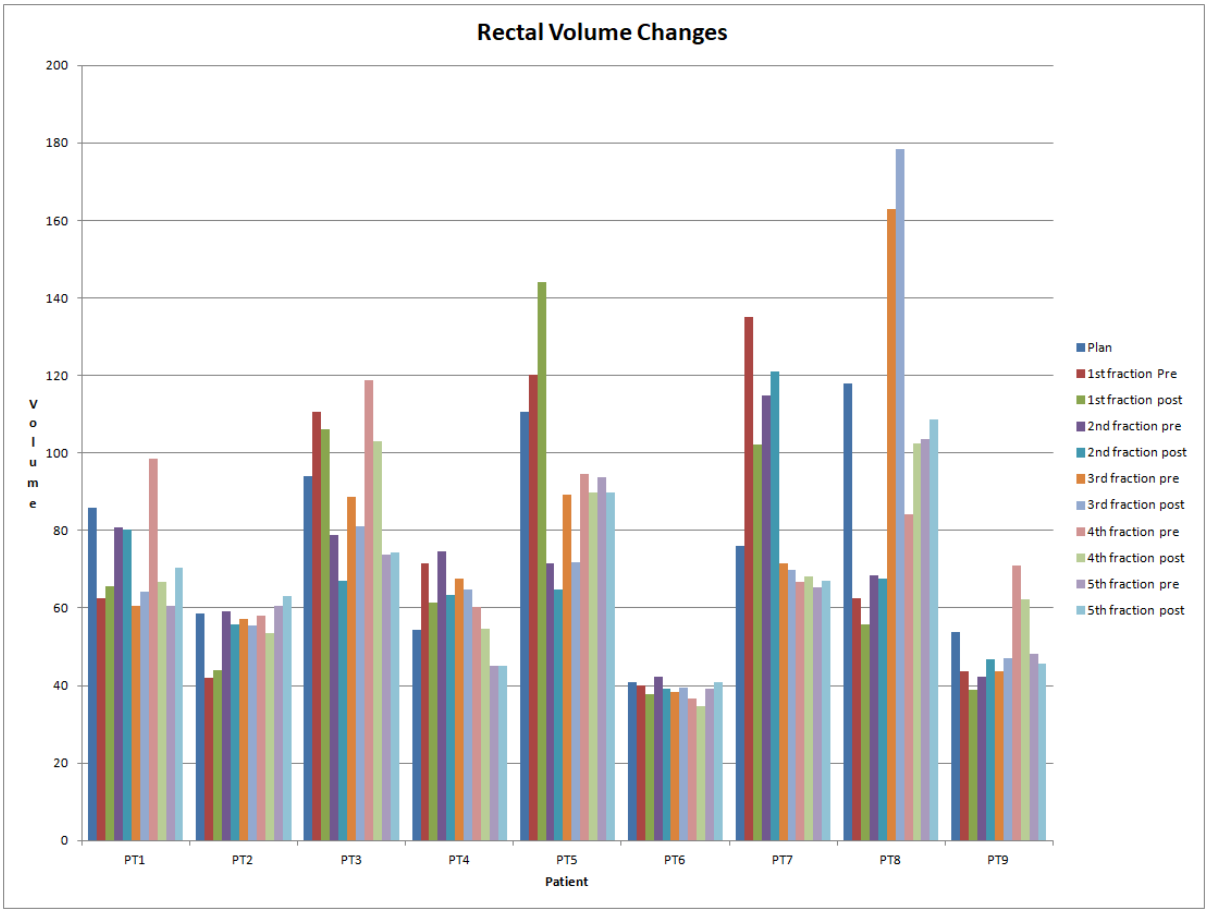
Methods

A total of 90 on treatment CBCTs were analysed from 9 sbrt prostate patients treated as part of a local clinical trial. All Rectal volumes were outlined, by one individual, for all 9 patients using the original planning CT image and each pre and post cone beam (CBCT) taken as part of the treatment delivery process. Treatment delivery time was recorded, as the time in minutes, between each pre and post treatment CBCT. Intra fraction rectal volume changes were noted with all on treatment volumes compared against the planned volume to again correlate any link with on treatment time. RTOG patient reported GI toxicity scores , recorded as per routine patient follow up, were used to assess any relationship between the on treatment observed variations and overall treatment related toxicity .

Results

Overall treatment was delivered between 11 and 39 mins. Of the 45 treatment sessions analysed a delivery time between 15-16 mins was the most common, occuring in 13 sessions, with the majority of sessions delivered between 14-18 mins overall (34 sessions). 2 sessions took over 30 mins to deliver, further investigation highlighted acute GU toxicity at these time points to be the cause. Figure 1 highlights the various treatment delivery times for each patient . Rectal volumes all varied from the initial planned volume, with rectal gas observed as the cause. No trends could be reported, concering this volume change , with random variations recorded both intra and interfractionally. Patient reported outcome data is displayed in table 1 . With the expection of one patient reporting a grade 3 acute toxicity , all other scores have been recored no higher than 1 .

FIG 1


Rectal Volume Changes
Volume
200
180
160
140
120
100
80
60
40
20
0
PT1
PT2
PT3
PT4
PT5
PT6
PT7
PT8
PT9
Patient
Plan
1st fraction Pre
1st fraction post
2nd fraction pre
2nd fraction post
3rd fraction pre
3rd fraction post
4th fraction pre
4th fraction post
5th fraction pre
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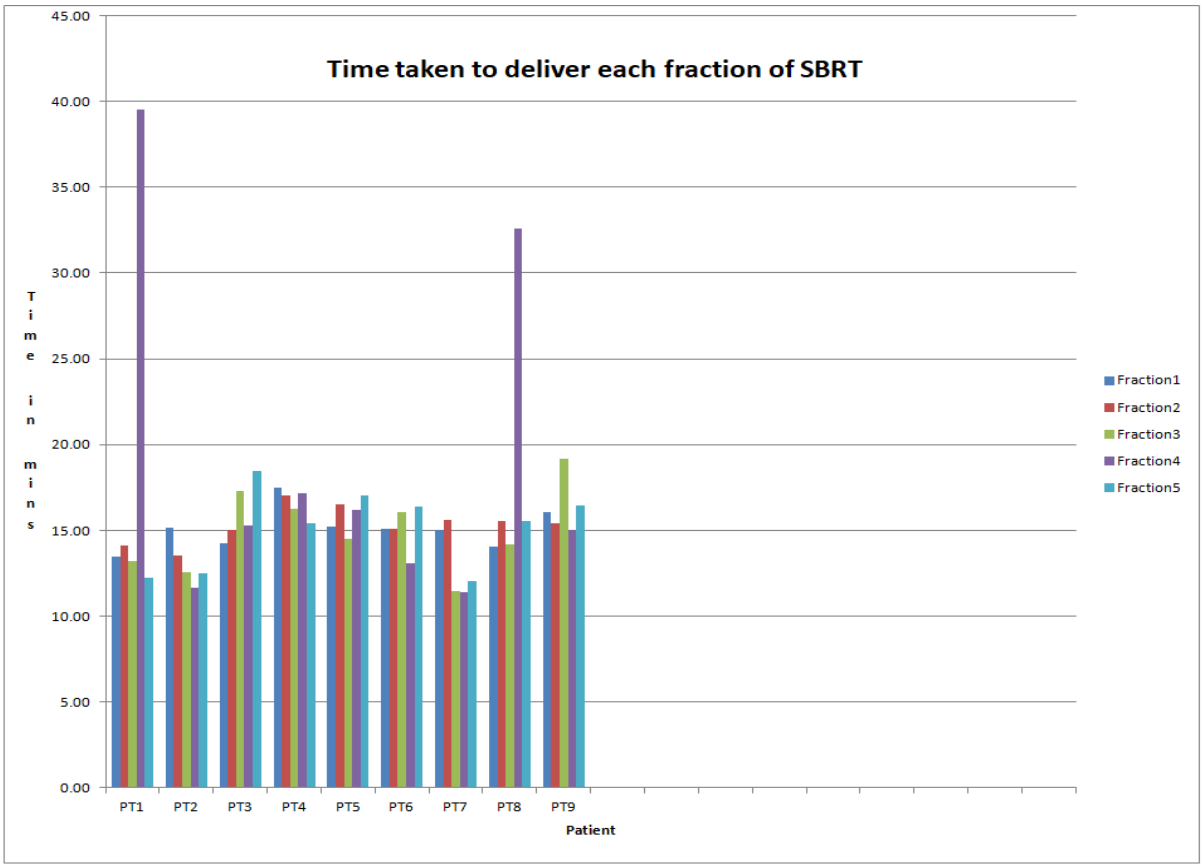
Time taken to deliver each fraction of SBRT
Time in mins
45.00
40.00
35.00
30.00
25.00
20.00
15.00
10.00
5.00
0.00
PT1
PT2
PT3
PT4
PT5
PT6
PT7
PT8
PT9
Patient
Fraction1
Fraction2
Fraction3
Fraction4
Fraction5

FIG 2

Table 1: Patient reported toxicity scores

	RTOG Gastrointestinal tox					
	wk6	wk12	6mnths	12mnths	18mnths	24mnths
PT1	1	0	0	0	0	0
PT2	1	0	0	0	0	0
PT3	1	1	0	RIP	RIP	RIP
PT4	0	0	1	1	0	
PT5	1	1	0	0	0	
PT6	1	0	0	1	0	
PT7	1	0	0	0		
PT8	3	1	1	0		
PT9	1	1	0	0		

Conclusion

In this cohort of patients observed initial analysis does not highlight any association between increased treatment delivery time and overall higher patient reported toxicity scores . Although rectal volumes fluctuated throughout again this study has found no correlation between rectal volume change and overall treatment delivery time . It is hoped further dosimetric evaluation, using DVH analysis, will further evidence that on treatment time is independent of associated treatment toxicity and aid in the essential,clinical on treatment decision making process of the RTT.

Session 2 – Optimising Radiotherapy for Lung Cancer Patients

Cell-free and circulating tumour DNA as a biomarker in patients receiving stereotactic ablative radiotherapy for early-stage lung cancer

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Background

Tumour-specific mutations in cell-free DNA (cfDNA) can provide valuable genomic information in patients without a molecular diagnosis from tumour tissue. We hypothesised that clinically relevant tumour-derived mutations can be detected in the cfDNA of patients undergoing stereotactic ablative body radiotherapy (SABR) for early-stage lung cancer. Differences in total plasma cfDNA concentration between patients who developed early disease progression and progression-free patients were also evaluated.

Methods

Recruited patients received SABR (55Gy in 5 fractions) for stage IA disease. Blood samples were taken before, during and after completion of SABR. Total plasma cfDNA concentration was quantified in all samples. As a proof-of-concept study, panel-based ultra-deep sequencing (35,000x; TSO500 Illumina liquid biopsy assay) was carried out on the pre and during (and 4 weeks post-treatment in one patient) SABR samples in a sub-cohort (n=3). Patients' electronic records were used to determine if they had developed disease progression by the time of follow-up (median follow-up: 15.3 months).

Results

24 patients with T1a – T1cN0M0 disease were recruited. Ultra-deep sequencing of cfDNA of three patients identified 49 somatic mutations. In one patient, the *EGFR* missense mutation G305S of likely pathogenic significance was identified in pre- and post-SABR cfDNA. In the whole cohort, median cfDNA concentration was non-significantly higher in the disease-progression group (n=4) at every time point. Kaplan-Meier analysis of cfDNA concentration approximately 30 minutes after fraction 1 showed a significant difference in median progression-free survival above and below a concentration of 5.8ng/ml (12.0 months vs. not reached, $P = 0.003$. HR: 13.39, 95% CI: 1.06-168.9).

Conclusions

Ultra-deep sequencing of circulating DNA can identify somatic mutations in cfDNA released by early-stage lung tumours, that could potentially help guide treatment decisions. Analysis of cfDNA during SABR for early-stage lung cancer showed preliminary evidence that cfDNA concentration may identify patients at higher risk of early treatment failure.

Hypoxia PET/CT – Investigating a Potential Biomarker for Radiotherapy

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Hypoxia is a well-recognised tumour characteristic that can adversely affect radiotherapy outcomes in most solid tumour types. However, it is not currently routinely assessed as part of the initial investigations pre-treatment for any solid tumour, nor is treatment routinely adjusted to account for hypoxia. Radiotherapy dose escalation and adaptive radiotherapy provide the potential for personalisation of radiotherapy, adjusted for hypoxic regions.

It is key therefore to establish a means of identifying hypoxia in tumours reliably and as part of a patient's standard management. Traditional methods for assessing tumour hypoxia are often invasive and not easily adaptable to the clinical setting. Positron Emission Tomography (PET) hypoxia radiotracers specifically localise in hypoxic cells and offer a non invasive, three dimensional assessment of tumour hypoxia. This presentation will focus on the hypoxia PET/CT tracers FAZA and F-MISO, and look at both laboratory and clinical methods to help determine whether hypoxia PET/CT can be validated as a reproducible biomarker, truly representative of the intratumoral environment and oxygenation levels.

Overview of PhD Findings – Re-Irradiation for Lung Cancer

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Lung cancer is the most lethal malignancy in the UK, with over 45,000 people diagnosed each year, and over 39,000 deaths. Of those suitable for radical treatment, it is estimated that approximately 45% of lung cancer patients will have a course of radiotherapy to their chest as part of initial treatment. Unfortunately, conventionally fractionated radiotherapy has a local recurrence rate of 20-30% of patients with non-small cell lung cancer (NSCLC). In addition, there is a risk of a second primary lung cancer (the risk of which is 14% over 10 years after initial treatment). It is estimated that 700 patients annually in the UK have local recurrence or a metachronous lung cancer, yet there are no guidelines about how to treat this group.

Radical re-irradiation has been given to patients since the 1970s, but is now increasing in use. Concerns about re-irradiation focus in two key questions: what dose of radiation can normal tissues tolerate at second treatments before causing high-grade toxicity and; how will re-irradiation overcome radioresistant cancers? This presentation will focus of the former question, detailing recent research on re-irradiation dose constraints and guidance on the appropriate patients for re-irradiation, and how to deliver re-treatment safely. It will conclude with an overview of the work in progress to discover the efficacy of re-irradiation.

Improving Patient Fitness for Lung Cancer Treatment

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Treatment options for stage 3 Non-Small Cell Lung Cancer are increasing, leading to improved survival for those receiving optimal treatment. However, treatment rates with combined chemo-radiotherapy across the UK vary significantly and are low overall.

The aim of this talk is to discuss the possible reasons for this, analysing biomarkers of poor outcome. Understanding how those at risk of a poor outcome could be identified is vital and appreciating how their fitness could be improved, with the aim of improving treatment rates and subsequent overall survival.

Session 3 – Optimising Radiotherapy for Head & Neck & Brain Cancer Patients

Using Radiomics to Personalise Radiotherapy for Head & Neck and Prostate Cancer

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The widespread implementation of IMRT, ever-improving image guidance, and a greater focus on accurate, precise, and homogeneous contouring practice have all led to significant improvements in radiotherapy for both prostate, and head-and-neck cancer in recent years. However, treatment regimens for tumour sites are population based, and have changed slowly over this time. Furthermore, radiation dose-based predictive models of both disease-control (TCP) and long-term side effects (NTCP), are relatively crude. In head and neck cancer, NTCP models predict late swallowing dysfunction, xerostomia, and taste disturbance with 70-80% accuracy at the population level, but are less good at predicting risk for a given individual. Therefore, in the era of personalised medicine, radiation oncologists are looking for new tools that will improve our ability to quantify these risks, and make nuanced data-driven decisions for patients.

Radiomics is a data-mining technique that extracts large numbers of imaging features from routine medical imaging, and uses these features to improve clinical decision-support systems. In head and neck cancer, adding radiomics features derived from diagnostic imaging to standard dose-based NTCP models has been shown to improve prediction of late toxicity following radiotherapy. In the IMAGE-INE project, we are extending this methodology by extracting features from image-guidance scans, hypothesising that these images contain hitherto untapped information about individual patient radiosensitivity that could improve predictive models. In the PROSECCA project, we intend to deploy this methodology at scale for patients who have had radiotherapy for prostate cancer across Scotland. Initially limiting our analysis to patients treated with IMRT from 2011 (N=11,000), we will combine clinical, dosimetric and radiomics features into multi-dimensional variable matrices, and use cutting edge machine-learning analysis to improve our ability to predict response at the level of the individual, and improve our ability to personalise treatment for our patients.

Feasibility of Dose Escalation in Head and Neck Cancers with Multi-Criteria Optimisation

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Background

The incidence of oropharyngeal squamous cell cancer (OPSCC) has increased significantly worldwide. Despite patients receiving intensive radical radiotherapy, the invasive nature of this malignancy results in high loco-regional recurrence rates. Following the MeRIno clinical trial, which studied whether a predictive biomarker could be established using diffusion weighted MRI imaging to identify patients who respond poorly to radiotherapy, this study aims to assess whether increasing the delivered radiotherapy dose to the gross tumour volume (GTV) to 73Gy and 82Gy half-way through treatment is feasible without increasing PTV doses considerably and still achieving acceptable organs at risk (OAR) doses.

Materials and Methods

Twenty representative patients (HPV-, smokers) with high risk, locally advanced OPSCC, were re-planned retrospectively using Eclipse TPS v15.5, RapidPlan® (RP) and multi-criteria optimisation (MCO). At our centre, OPSCCs are typically prescribed 65Gy in 30# to the high risk planning target volume (PTV65) while the low risk volume (PTV54) is treated to 54Gy in 30#. The original clinical plans were re-optimised with a locally published RP model and MCO (Group I). These plans were then used to escalate the dose to the GTV to 73Gy (Group II) and 82Gy (Group III). The re-optimised clinical plans were split into two phases of 15# each. Phase 1 consisted of 1-15# set to 2.17Gy/#, while Phase 2 consisted of 16-30# set to 2.70Gy/# or 3.30Gy/# to simulate dose escalation for the remaining 15#. Plan sums were created for a total of 30#. A number of plan evaluation parameters were recorded along with assessments of plan deliverability.

Results and Conclusion

This planning feasibility study exploring RP combined with MCO has, rather promisingly, enabled the dose to the GTV to be escalated by 12.3% and 26.2% to 73 and 82Gy, respectively, without significantly increasing mean PTV or OAR doses. As evidence shows that recurrences most often occur in the GTV, dose escalation has the potential to treat high risk patients more effectively in the first instance and is likely to be safe due to comparable OAR doses currently administered

Hippocampal Sparing for Low Grade Glioma

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Radiotherapy (RT) plays an integral role in the management of Low-Grade Gliomas (LGG). Late toxicity from RT can result in worsening neurocognitive function. Radiation-induced damage to the hippocampus (HPC) plays a considerable role in memory decline. Advancements in photon planning software have resulted in the development of multi-criteria optimization (MCO) and HyperArc. These new technologies may improve HPC sparing while maintaining PTV target coverage.

Study Objective

To compare 3 different hippocampal sparing (HS) planning techniques for Low Grade Gliomas.

Materials and Methods

LGG patients were retrospectively identified from 2015-2019. All patients were originally planned with VMAT. Dose prescribed was 50.4Gy/28. Target volumes were delineated as per departmental guidelines. The HPC was retrospectively delineated as per the RTOG 0933 atlas by two neuro-radiologists. VMAT plans were optimised to reduce the dose to the HPC without compromising other parameters, in particular the PTV. The comparative planning methods are; VMAT without HS (VMAT); VMAT with HS (VMAT-HS), VMAT-MCO with HS (VMAT-MCO); HyperArc with HS (HyperArcPlans were assessed for PTV coverage and the following dose metrics to hippocampus; D40%, Max and Mean.

Results

25 patients were identified. The contra lateral HPC was spared in 16 patients and both HPC in 9. All three HS planning techniques showed significant dose reductions of the spared HPC in both contra-lateral and bilateral cases ($p < 0.05$). VMAT-MCO and HyperArc are superior to VMAT-HS in lowering the dose to contra lateral HPC in all measured metrics ($p<0.05$) but not with bilateral HPC sparing. PTV coverage was achieved for all plans

Conclusion

VMAT-HS, VMAT-MCO and HyperArc result in superior HS compared to VMAT. In patients where only the contra lateral HPC can be spared, VMAT-MCO and HyperArc are superior to VMAT-HS.

Patient Compliance with Prostate Radiotherapy Planning Protocols – Can we do Better?

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Background

Maintaining organ consistency is integral in addressing randomised error during radiotherapy treatment. To accomplish this, departmental protocol requires patients use micro-enemas followed by drinking 500mls water 30 minutes before scanning achieving a bladder volume >100mls and rectum <4cm. These instructions are delivered to patients verbally at clinic and in booklets. Ineffective preparation can result in multiple hospital attendances and treatment delays.

Aims/Objective

Assessing the impact on rescan rates of providing education to patients on preparation protocols via telephone prior to planning scans for prostate radiotherapy.

Methods/Results

Between October 2019 and October 2020, 554 prostate patients underwent a planning CT scan where 19.9% required rescanning; 10.7 % due to small bladder size and 9.2% with rectal distension. Subsequently, 50 patients were telephoned up to 10 days before scanning, to advise drinking 2 litres of water daily to increase hydration, and educated on enema usage the night before and morning of scanning. 50 patients were assessed, however 9 (18%) were non contactable with 3 (33.3%) requiring a rescan; 2 (22.2%) due to insufficient bladder size and 1 (11.1%) with rectal distension. 5 (12.2%, 95% CI, 4.1-26.2%) contactable patients required rescanning; 4 (9.8%) due to insufficient bladder volume and 1 (2.4%) due to rectal distension. In total, rescans were required in 16.0% (95% CI, 7.2-29.1%) of all 50 patients.

Conclusion

Preliminary results suggest contacting patients prior to radiotherapy planning appointments can reduce rescan rates, although not to statistical significance. To prove conclusive, larger sample size is required therefore this study is ongoing.

Low-Dose Lung Radiotherapy for COVID-19 lung disease: Preclinical Studies in a Bleomycin model of Pneumonitis

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Background

Clinical studies examining the use of low-dose lung radiotherapy (LDLR) for the treatment of COVID-19 pneumonitis are underway, despite intense controversy. The current lack of pre-clinical investigations to inform trial design has created an urgent need for such data.

Objectives

Using an inhaled-bleomycin mouse model of pneumonitis, which reproduces many of the pathophysiological changes observed in COVID-19, we aimed to examine LDLR efficacy, optimal dosing and mechanism of action.

Results

Mice treated with bleomycin (11.25 units/kg) and then exposed to LDLR (1 Gy) on day 3 were monitored for a further 7 days. Recovery of bodyweight following exposure to bleomycin was enhanced in a subset of mice that received LDLR. Defining recovery as a return to at least 98% of initial bodyweight revealed that LDLR-treated mice (21.2%) had a significantly enhanced probability of recovery compared to sham irradiated subjects (3.3%, P=0.03). Accordingly, a proportion of mice treated with LDLR exhibited less severe histopathological lung changes. Treatment with LDLR was also associated with significantly less deterioration of aerated lung volume on CT imaging (4.1%) compared to sham irradiated mice (10.0%, P=0.02). Mechanistically, LDLR was found to significantly inhibit bleomycin-induced increases in interstitial macrophages (P=0.009), CD103+ dendritic cells (P<0.001) and neutrophil-DC hybrids (P=0.05) in the lung. Other doses of LDLR (0.5 and 1.5 Gy) are also under investigation.

Conclusions

Evidence of the efficacy of LDLR (1 Gy) in less severe cases of pneumonitis, associated with suppression of immune cell recruitment, supports its investigation in the clinical setting.

Does Inter-Observer Variation Affect Functional Imaging Quantification in DW-MRI for HNSCC?

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Background

Apparent diffusion coefficient (ADC) measured using diffusion-weighted (DW)-MRI as an imaging biomarker, may allow delivery of personalised, biologically adaptive radiotherapy (RT) for head and neck cancer (HNC).

Aims

This work aims to evaluate the impact of inter-observer variation (IOV) on delineated target volumes and measured ADC on the ADC map generated from DW-MRI.

Methods

MRI scans were acquired at baseline (MRI_1) and #10 (MRI_2) of RT. Gross target volume (GTV) delineation and ADC measurement of primary (GTVp) and lymph node (GTVn) disease was undertaken on both scans. A radiographer and clinical oncologist (CO) manually delineated the structures on the T1 post contrast fat saturated (T1PCFS) sequences. The gold standard was a delineation of each target volume by the CO amended or verified by the radiologist (RO).

Mean differences and standard deviations of GTVs were measured between observers. IOV was evaluated using paired t-tests and repeated measures ANOVA. Concordance in delineation of volumes was assessed using Dice Similarity Coefficient (DSC).

Results

GTVp and GTVn contours from MRI_1 and MRI_2 were assessed in ten patients (20 MRI scans with 49 lesions).No statistically significant differences in mean volume for GTVp ($p=0.31$) or GTVn ($p=0.98$) between the observers was detected.

The DSC between the radiographer and CO on the T1PCFS was 0.66 (SD 0.16) for GTVp and 0.81 (SD 0.12) for GTVn. The radiographer DSC with the gold standard volumes was 0.64 (SD 0.25) and 0.83 (SD 0.14) for GTVp and GTVn, respectively.

No significant difference in mean ADC (baseline $p=0.55$, repeat $p=0.36$) or % change in ADC ($p= 0.91$) was detected between observers.

Conclusions

Moderate DSC was demonstrated with higher agreement for nodal outlines than primary tumour. The measured mean and % change in ADC was not significantly different between observers. Radiographer led evaluation of ADC using DW-MRI during RT for HNSCC is feasible.

Initial Findings of an International Delphi Consensus Study Regarding the Optimal Management of Radiation Pneumonitis

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Background

There is a lack of consensus in the diagnosis, management and follow-up of radiation pneumonitis (RP). A Delphi consensus process was conducted in this area.

Methods

In round 1, open questions were distributed to 31 clinicians treating thoracic malignancy. In round 2, participants rated agreement/disagreement with derived statements using a 5-point Likert scale. Consensus was defined as =75% agreement. A final round to establish consensus in unresolved areas is underway.

Results

Response rate was 74% in round 1 (n=23/31; 17 oncologists, 6 respirologists); 82% in round 2 (n=19/23; 15 oncologists, 4 respirologists). 38/64 round 2 statements attained =75% agreement. There was agreement that risk stratification/mitigation should consider patient factors (ILD, autoimmune/connective tissue disease, COPD/emphysema, previous chemotherapy/radiotherapy, PS, lung function, smoking status); minimising RP risk through treatment planning (reducing PTV margins, normal lung dose; 4DCT, respiratory gating, breathhold techniques, IMRT/VMAT, daily imaging; meeting constraints for V20, MLD); diagnosis should be based on symptoms, exam, temporal relationship to treatment, CT imaging, exclusion of other causes and common toxicity grading scales; treatment of RP should involve oncologists and respirologists, and should involve oral steroids with consideration of gastroprotection, starting with 60mg PO prednisolone or equivalent, for a duration of 2 weeks, with a taper of 10mg in the daily dose per week, or for severe pneumonitis, IV methylprednisolone for 3 days before PO; and that it would be helpful to develop radiation pneumonitis guidelines.

Conclusions

Consensus was achieved on many aspects of RP diagnosis and management. Further consensus may be possible.

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