Materials and Methods:

Volumes.

Biomarkers and could potentially be extended to imaging bulk 3D.

Present a technique that enables simultaneous imaging of multiple

Receptors, thus acting as biomarkers for tumour characteristics. We

With antibodies that enable cellular uptake via specific cellular

Contrast agent for tumour characteristics; NPs can be functionalised

Angiogenesis). We investigated the use of nanoparticles (NPs) as a

Radiosensitivity information (hypoxia, proliferative ability and

Technique sensitive to tumour characteristics that gives

Collagen type 1 to construct 3D.

In vitro cancer models to demonstrate

Purpose/Objective: There is a clinical need for a functional imaging
technique sensitive to tumour characteristics that gives radiosensitivity information (hypoxia, proliferative ability and angiogenesis). We investigated the use of nanoparticles (NPs) as a contrast agent for tumour characteristics; NPs can be functionalised with antibodies that enable cellular uptake via specific cellular receptors, thus acting as biomarkers for tumour characteristics. We present a technique that enables simultaneous imaging of multiple biomarkers and could potentially be extended to imaging bulk 3D volumes.

Materials and Methods: We have devised an x-ray fluorescence (XRF) technique capable of imaging NP concentration. The novel XRF imaging module consisted of a focussing polycapillary optic coupled to an energy resolving silicon drift detector. Proof of concept imaging to distinguish two component metals was undertaken; a phantom consisting of gold and tantalum wires was constructed and imaged. Demonstration of sensitivity to NP uptake in cells was performed; this involved NP cellular uptake experiments with colorectal cancer cells (HT29) and stromal cells (fibroblasts 3T3) using varying incubation time.

Results: The technique demonstrated ability to distinguish two metal types in imaging mode. XRF imaging was performed of several slices of the 3D cancer model (with a challenging GNP concentration ratio of 5:1 between the tumour mass (0.7 million HT29) and surrounding) and all component details could be clearly seen, with a delineated tumour mass emitting at 5x more than the surrounding cellular stroma (Fig 1). The XRF signal was linear with NP concentration down to GNP concentrations of 1ppm.

Conclusions: The positive correlation between ADC and ve can partly be explained by considering that extracellular diffusion is higher than intracellular diffusion. Since ve is a measure of the extracellular extravascular volume fraction a positive correlation with ADC was expected. In other words, the water molecules are able to traverse a greater distance resulting in a greater ADC value when the space not occupied by cells or vessels (ve) is high. However, in median, only 4% of the variation in ADC can be explained by ve. Similarly, RS90 only explains in median 2.4% of the variation in ADC for this population. Inhomogeneities in the static B0-field may lead to distortions of the ADC maps. These B0-field correction was not taken into account in the analysis and may influence the correlation between ADC and perfusion-parameters. The time between the DW-MRI and the DCE-MRI is around 20 min and in this time the correlations may be deteriorated by motion and changes in the microenvironment of the tumor. To conclude, it may be said that DW-MRI and the DCE-MRI are mainly supplying complementary information about the tumor micro-environment.

OC-0153

A quantitative technique for simultaneous imaging of multiple biomarkers.

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Purpose/Objective: There is a clinical need for a functional imaging technique sensitive to tumour characteristics that gives radiosensitivity information (hypoxia, proliferative ability and angiogenesis). We investigated the use of nanoparticles (NPs) as a contrast agent for tumour characteristics; NPs can be functionalised with antibodies that enable cellular uptake via specific cellular receptors, thus acting as biomarkers for tumour characteristics. We present a technique that enables simultaneous imaging of multiple biomarkers and could potentially be extended to imaging bulk 3D volumes.

Materials and Methods: We have devised an x-ray fluorescence (XRF) technique capable of imaging NP concentration. The novel XRF imaging module consisted of a focussing polycapillary optic coupled to an energy resolving silicon drift detector. Proof of concept imaging to distinguish two component metals was undertaken; a phantom consisting of gold and tantalum wires was constructed and imaged. Demonstration of sensitivity to NP uptake in cells was performed; this involved NP cellular uptake experiments with colorectal cancer cells (HT29) and stromal cells (fibroblasts 3T3) using varying incubation times of 1.9 nm gold NPs. The NP loaded cells were nested in collagen type 1 to construct 3D in vitro cancer models to demonstrate the sensitivity of the XRF technique to NP concentration and distribution.

Results: The technique demonstrated ability to distinguish two metal types in imaging mode. XRF imaging was performed of several slices of the 3D cancer model (with a challenging GNP concentration ratio of 5:1 between the tumour mass (0.7 million HT29) and surrounding) and all component details could be clearly seen, with a delineated tumour mass emitting at 5x more than the surrounding cellular stroma (Fig 1). The XRF signal was linear with NP concentration down to GNP concentrations of 1ppm.

Conclusions: The positive correlation between ADC and ve can partly be explained by considering that extracellular diffusion is higher than intracellular diffusion. Since ve is a measure of the extracellular extravascular volume fraction a positive correlation with ADC was expected. In other words, the water molecules are able to traverse a greater distance resulting in a greater ADC value when the space not occupied by cells or vessels (ve) is high. However, in median, only 4% of the variation in ADC can be explained by ve. Similarly, RS90 only explains in median 2.4% of the variation in ADC for this population. Inhomogeneities in the static B0-field may lead to distortions of the ADC maps. These B0-field correction was not taken into account in the analysis and may influence the correlation between ADC and perfusion-parameters. The time between the DW-MRI and the DCE-MRI is around 20 min and in this time the correlations may be deteriorated by motion and changes in the microenvironment of the tumor. To conclude, it may be said that DW-MRI and the DCE-MRI are mainly supplying complementary information about the tumor micro-environment.

OC-0154

A comparison of the gamma index sensitivity in various commercial IMRT/VMAT QA systems.

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Purpose/Objective: QA for IMRT and VMAT has evolved substantially. In recent years, various commercial 2D and 3D ionization chamber or diode detector arrays have become commercially available, allowing for absolute dose verification with near real time results. This has led to a wide uptake to replace point dose and film dosimetry and to facilitate QA streamlining. However, arrays are limited by their spatial resolution which may affect the sensitivity of the gamma index analysis. The purpose of this study was to compare the sensitivity of the gamma index analysis (γ) in the Delta4®, ArcCHECK®, PTW 2D-Array seven29™ and Octavius II™ phantom combination, Gafchromic® EBT2 and composite Varian Portal Dosimetry EPID measurements.

Materials and Methods: To evaluate the sensitivity of the different systems, errors were designed with deliberate changes of 1, 2, 5mm introduced into prostate and head & neck IMRT and RapidArc™ plans throughout all control points in all fields for one 5mm MLC leaf. Collimator rotation errors of 1, 2, and 5° were introduced into prostate and head & neck IMRT and RapidArc™ plans. The expected gamma index pass rate was simulated by exporting the normal plan predicted dose and the calculated dose from each system. The predicted y was calculated in Versisoft v5, OmniPro I’mRT v7, Delta4 software, SNC Patient v6, Portal Dosimetry v10, and averaged. Measurements were evaluated against the unperturbed dose distribution calculated using Varian Eclipse®: the relevant phantom. In all cases, global y was used with a 20% threshold relative to a point selected in a high dose and low gradient region. Various criteria for γ were analysed, including the commonly used 3%/3mm criteria. The ρ based on measurement was compared against the predicted to evaluate the sensitivity of each system. The concordance correlation coefficient, ρ, was used to assess statistical agreement.

Results: There was good agreement between the predicted γ from each software (all ρ=0.93 relative to the average prediction). A
OC-0155

Pre-treatment verification of VMAT dose delivery as a function of gantry angle using EPID

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Purpose/Objective: The use of volumetric arc therapy (VMAT) is growing rapidly for many radio-therapy treatments due to its ability to quickly deliver highly conformal dose distributions. There has also been an increasing interest to use high dose rate flattening filter free (FFF) beams as inverse planning systems do not require flat, evenly distributed beams. Such fast and complex treatments should be accompanied by robust verification. Methods to calibrate electronic portal imaging device (EPID) dosimetry has been previously documented for step and shoot stereotactic treatments such as intensity modulated radiotherapy (IMRT) using only flattened beams and only on the integrated fraction or beam. The aim of this work is to provide a time-dependent dose verification method for VMAT that can be used with flattened or FFF pre-treatment beams via a general calibration model for amorphous silicon (a-Si) EPIDs.

Materials and Methods: The general calibration model was created using a Varian TrueBeam, equipped with an as1000 EPID, for each unique energy spectrum 6MV, 10MV, 6MV-FFF, 10MV-FFF taking the field size, off axis ratio, and penumbral spectral changes of the beam into account. Also included in the model are the EPID specific corrections such as pixel sensitivity, support arm back scatter, and image ghosting. As planned VMAT treatments are separated into control points (CPs) for optimization, measured images are also separated into the same time intervals so that direct verification of prediction images can be performed. Linac log files were used to synchronize measurement and prediction. The dosimetric accuracy of the calibration model was determined for a range of treatment conditions. Measured and predicted 2D control point doses were compared using a gamma evaluation with criterion of 3%/3mm. Results: Of 20 VMAT plans tested that passed the clinical action level for integrated dose (95% in field area with gamma within 3%/3mm), the poorest performing plan contained 4.2% in-field area failing the gamma criterion when delivered with a flattened beam and 4.0% of the same plan, the highest dose variation in delivery of FFF plans was -0.5% compared to 0.2% for flattened beams.

Conclusions: The EPID calibration model allows verification of pre-treatment VMAT doses for both flattened and unflattened beams in a time-dependent manner.