

## The relationship between absorbed dose and DNA damage in lymphocytes after radionuclide therapy

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Rapid Arc. 4) PF test during RapidArc with intentional errors. 5) Accurate control of dose rate and gantry speed during RapidArc delivery. 6) Accurate control of leaf speed during RapidArc delivery. These RapidArc QA plans were loaded on Machine and analysed using EPID portal dosimetry system.

**Results and Discussion:** Taking DMLC dosimetry, we measured meter reading at gantry angles 0°, 180°, 90° and 270° for a 4x10 cm DMLC field with a 0.5 cm slit, and the effect of gravity on leaf position and linac head showed maximum percentage deviation of -0.96% ( $\pm 2\%$ ). PF test at stationary gantry angles 0°, 180°, 90° and 270°, we evaluated the maximum DMLC positional shift of 0.5mm ( $\pm 1$  mm). PF test during RapidArc (arc 179°-187°) has inspected the effect of gantry rotation on the MLC position, the result showed a maximum positional shift of -0.2 mm ( $\pm 1$  mm). PF test during RapidArc with intentional errors have demonstrated that the test (3) can detect sub-millimetre errors during RapidArc. Accurate control of dose rate and gantry speed during RapidArc delivery has been examined by using 7 combinations of dose-rate, gantry range and gantry speed to give equal dose to seven 1.8 cm strips in a RapidArc field. When normalised to open field at same position (to exclude the beam profile influence), the dose of seven strips showed good result, with maximum mean deviation of 1.90% ( $< 2\%$ ). Accurate control of leaf speed during RapidArc delivery has been analysed by using 4 combinations of leaf speed (1.6, 2.4, 0.8 and 0.4 cm/s) and dose-rate to give equal dose to four strips in a RapidArc field. When normalised to corresponding open field, the dose of four strips showed good result, with a maximum mean deviation of 1.74% ( $< 2\%$ ). All the test results showed good agreement with manufacture and published literature stated tolerance values (written in bracket in front of each result). The RapidArc commissioning data has also obtained an approval from Atomic Energy Regulatory Board (AERB), Mumbai, India.

**Conclusion:** The dosimetric verification of DMLC movement, variable dose rates and gantry speed provides confidence over precision and accuracy during RapidArc delivery. These test are aimed only for commissioning and dosimetric verification of RapidArc enabled linac, and not for patient specific QA.

**Keywords:** Dosimetry, EPID, DMLC.

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#### Dosimetric Measurement for Isocentre Blocked Boost Fields in 3D-CRT Treatment Plans

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**Purpose:** Boost fields (A small field with isocentre blocked and less beam weightage) are routinely used in three dimensional conformal radiotherapy (3D-CRT) treatment plans of oesophagus, head and neck etc for enhancing PTV coverage. Challenges for using boost fields are associated with accuracy of treatment planning system (TPS) to calculate dose distribution, normalisation and monitor units (MUs) as isocentre is blocked so dosimetric verification of boost field is essential. The purpose of this study was to measure two things; first contribution of 'Boost fields' doses to the target isocentre, second doses to the region of interest of boost field and finally compare the dosimetrically measured data with TPS calculated data.

**Materials and Methods:** Eclipse TPS (Version 8.6, Varian) was used for all boost fields 3D-CRT treatment plans in this study. The solid water phantom with dimension (25cmx25cmx5cm), (25cmx25cmx2cm) and (25cmx25cmx5cm) respectively was used. The 0.65cc ionisation chamber was used for dosimetry in this study with SAD (source axis distance) setup. In boost fields study, five treatment plans of oesophagus case each having two plans with 6MV and 15MV and each plan having two boost fields (one is LPO boost field and other is RPO boost field) were performed. The contribution of boost field doses to the target isocentre for both 6MV and 15MV plans

were measured with the help of ionisation chamber and also calculated in treatment planning system. The doses to the region of interest of boost field at 5cm depth in phantom were measured with help of thermoluminescence detector (TLD-100) and also calculated in treatment planning system for both 6MV and 15MV plans. Finally the measured and calculated data was compared.

**Results:** Mean percentage variation between TPS calculated and ionisation chamber measured boost field doses to the target isocentre was 1.53% (SD 4.12) for 6MV and 4.13% (SD 6.81) for 15MV. Maximum Percentage variation for this was 6% and 12% for 6MV and 15MV respectively. Mean percentage variation between TPS calculated and TLDs measured boost field doses of region of interest of boost field was -1.22% (SD 2.03) for 6MV and -0.4% (SD 2.84) for 15MV. Maximum percentage variation for this was 4% and 5% for 6MV and 15MV respectively. TLDs were in good agreement with TPS. Results shows that contribution of boost field doses to the target isocentre for both 6MV and 15MV were less than 1cGy.

**Conclusion:** Dosimetric verification of MUs delivered by boost fields is essential to verify the accuracy of TPS algorithms.

**Keywords:** Boost Field, 3D-CRT, Isocentre

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#### The relationship between absorbed dose and DNA Damage in Lymphocytes after radionuclide therapy

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**Purpose:** In radionuclide therapy today mostly  $\beta^-$ -labelled radiopharmaceuticals are used which irradiate the body internally with time-dependent dose-rate and can cause DNA double strand breaks (DSBs).

The formation of a DNA DSB in nuclear chromatin results in the rapid phosphorylation of the histone variant gamma-H2AX. DSBs also recruit the damage sensor 53BP1 to the chromatin surrounding the DSBs, which leads to 53BP1 and gamma-H2AX co-localization. By immunofluorescence staining with gamma-H2AX and 53BP1 antibodies those biomarkers can be addressed by microscopically visible foci.

The number of foci per cell represent a quantitative biomarker for DNA double strand breaks and hence for radiation exposure and radiation effects. Presently, there are only few studies, which are studying the on-set and decay of DSBs after radionuclide therapy.

The aim of our study was, therefore, to generate an in-vitro calibration curve for quantifying the dose-response of the number of radiation induced foci (RIF) after internal irradiation of blood with  $\beta^-$ -emitters, and to describe comprehensively the dose-dependent time course of the DSB on-set and repair in lymphocytes of radiation treatment-naive patients after radiopeptide therapy with <sup>177</sup>Lu and radioiodine therapy with <sup>131</sup>I.

**Material and Methods:** For the in-vitro calibration with <sup>131</sup>I and <sup>177</sup>Lu blood samples were drawn from volunteers. Different activity concentrations were added, the samples were incubated for 1h to achieve absorbed doses up to 100mGy, and the number of RIF/cell was determined.

The patient studies addressed the relationship between the absorbed dose to the blood and the number and temporal behavior of radiation-induced DNA double strand breaks (RIF/cell) in multiple peripheral blood samples under radiopeptide therapy (16 patients) and under radioiodine therapy (20 patients).

**Results:** The in-vitro study shows that the number of RIF/cell is linearly dependent of the absorbed dose, similar to what has been observed after external irradiation.

In patients, the average number of RIF/cell showed a linear dose-response relationship within the first hours after administration of the radiopharmaceutical. Later time points were characterized by a diminishing number of radiation-

induced foci which was in accordance with the progression of DNA repair and the declining dose rates. The absorbed dose in most patients treated with  $^{131}\text{I}$  exceeded 20mGy in the first hour, and in these patients, the on-set of a fast repair component was observed.

**Conclusions:** With the experimental results and model calculations presented in this work, for the first time a dose-response relationship and a description of the time course of the in-vitro and in-vivo damage response after internal irradiation of  $\beta^-$ -emitters could be established.

**Keywords:** gamma-H2AX and 53BP1, radionuclide therapy, dosimetry

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#### **A quantitative assessment of intra-fractional tumor motion and deformation error on planned dose at conventional proton therapy**

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**Purpose:** In proton therapy, two major beam delivery techniques are used which are referenced as active and passive delivery strategies. In latter case, an effective dose distribution into tumor volume is created by pencil beam extracted from the accelerator exit window. To do this aim, the modulation is performed to produce two uniform beam profiles: 1) along with beam trajectory and 2) in lateral direction vertical to beam direction. The first dose profile cover tumor volume in target depth against beam direction and the second lateral profile include tumor volume, transversely. Several passive devices are utilized to create depth dose profile known as Spread-Out Bragg Peak (SOBP) and transverse dose profiles. In proton therapy, the final purpose is to produce a three dimensional (3D) homogeneous dose distribution onto the tumor volume while minimizing the dose to the surrounding healthy tissues around the tumor. Relating to moving and deforming targets, the delivery dose is not matched with the planned dose.

**Methods:** Our goal in this work is to obtain a quantitative assessment of three dimensional dose distribution on the moving and deforming targets and surrounding normal tissues affected by the breathing motion. For this aim, a simulation study was performed using Monte Carlo FLUKA code. The effect of each of the parameters in a clinical passive beam scanning system on radiotherapy dosage was considered. The dose deposition from protons was simulated for fields designed for the treatment of dynamic, deformed and static tumors.

**Results:** Dose distribution results of Monte Carlo method simulation were compared with the results obtained during experimental process at Cyclotron and Radioisotope Center (CYRIC) in Tohoku University. Final analyzed results represent that the uniformity of dose distribution on all given tumors are up to 95% of uniformity that proves a successful dose delivery onto tumor as well according to planned dose. The results of dose distribution into tumor and surrounding healthy tissues around the tumor for static spherical case regarding with deformed tumors and moving tumors were obtained. **Conclusion:** In conventional proton therapy a significant dose is delivered to the normal tissues in comparison with stationary condition without getting any strategy to limit ITV region such as motion gated or real-time tumor tracking strategies. The accuracy of dose distribution increasing with decreasing magnitude of deformation, moving and stretching of the tumor.

**Keywords:** Proton therapy, Radiotherapy Dosage, Monte Carlo Method.

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#### **A compact high current accelerator for radioisotope production**

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An initial design of a compact, high current Fixed Field Alternating Gradient accelerator has been made for the direct production of  $^{99m}\text{Tc}$  and the production of a number of therapeutic isotopes that currently available only in limited quantities or not at all. These studies indicate that the FFAG could in principle accelerate a proton beam of up to 20mA to at least 30 MeV and high current alpha beams to a similar energy. This presentation will describe the FFAG and show what radioisotope yields should be possible. It will also outline the next steps in the project. It should be noted that the same basic FFAG design is being extended to the energies required for cancer therapy with light ion beams.

**Keywords:** FFAG; high beam current; radioisotope production;  $^{99m}\text{Tc}$ ; therapeutic isotopes

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