Evaluation of breathing interplay effects during VMAT by using 3D gel measurements

S Ceberg¹, C Ceberg², M Falk³, P Munk af Rosenschöld³ and SÅJ Bäck¹
¹Department of Medical Radiation Physics, Lund University, Skåne University Hospital, Malmö, Sweden
²Medical Radiation Physics, Department of Clinical Sciences Lund, Lund University, Lund, Sweden
³Radiation Medicine Research Center, Department of Radiation Oncology, Rigshospitalet, Copenhagen, Denmark

E-mail: sofie.ceberg@med.lu.se

Abstract. Respiratory motion during dynamic radiotherapy may affect the absorbed dose distribution both by dose-reducing smoothing and by more complicated interplay effects. In this study we present a novel method to determine the relative importance of these two effects. For the two dynamic deliveries studied in this work, the expected target dose reduction due to the smoothing effect was estimated by measurements convolved by the motion function. Remaining absorbed dose differences were attributed to interplay effects between the motion of the gel phantom and the movement of the modulating MLC leaves during modulated arc radiotherapy. The total dosimetric effect due to breathing motion and dynamic MLC motion during VMAT delivery resulted in an average of about 4% target dose reduction. Comparing with only the smoothing effect, the average difference was decreased to around 1%, and the remaining distribution was attributed to interplay effects. Although the interplay effects were small compared to the smoothing effect, the standard deviations of 1.4-2.3% (1SD) were larger than the narrow distribution for repeated stationary measurement with a standard deviation between 0.5-0.9% (1SD).

1. Introduction
The desire to deliver high absorbed dose to the target volume while minimizing the dose to normal tissues during radiotherapy has resulted in advanced treatment procedures, for instance techniques using intensity modulated beams and arcs [1-3]. The advantages of these techniques are the increased possibility to deliver a high absorbed dose to the target volume while minimizing the dose to normal tissues. However, intra-fractional tumor motion, mostly due to respiration, can be a major challenge to the ambition to deliver the desired dose distributions.

Two types of dosimetric effects due to intra-fractional organ motion has been defined; A) the dose-blurring effect, where the dose delivered to a point in the patient is smeared by the motion of this point in the radiation beam, and B) the interplay effect, where the relative motion between the dynamic MLC leaves and the treatment region may lead to a more complicated dosimetric effect [4].

During a volumetric modulated arc therapy (VMAT) delivery the 3D trajectory of an MLC leaf is a combination of the gantry rotation and the MLC modulation. Investigations of potential breathing
interplay effects during this type of treatment delivery by experimental measurements using a high-resolution 3D-detector are highly desirable.

Using gel dosimetry, the absorbed dose can be obtained in the entire irradiated volume with high resolution [5, 6]. For example, a polymer gel dosimeter measures absorbed dose in over 10,000 measurement points in 3D for a target volume less than 5 cm³. It has been showed that polymer gel is a feasible detector for 3D dose verification of dynamic radiotherapy e.g. [7, 8].

The aim of this study was to investigate any potential breathing interplay effects during VMAT delivery by comparing absorbed dose measurements using 3D polymer gel. The interplay effect was defined as the difference between the absorbed dose volume measured during motion and the volume resulted from a stationary measurement convolved with the motion function. Thus, the blurring effect was subtracted from the measured dose volume during motion, which means that any residual dose differences are due to interplay effects.

2. Material and method

The gel preparation, read-out and data analysis were carried out at Lund University and Skåne University Hospital in Malmö while the VMAT treatment planning and delivery was carried out at Rigshospitalet in Copenhagen.

2.1. Polymer gel phantoms

The normoxic polyacrylamide gel (nPAG) used in this study contained 89% w/w ultra-pure deionised water, 3% w/w acrylamide, 3% w/w N,N’-methylenebisacrylamide, 5% w/w gelatine and 10 mM tetrakis(hydroxymethyl)–phosphonium chloride. Magnetic resonance imaging (MRI) using a 1.5 T unit (Siemens Symphony) was performed about 24 hours post-irradiation. The mixing- and read-out procedures are described elsewhere [8]. MATLAB 7.4.0 was used for image processing and 3D rendering. The R² data of the irradiated gel phantoms was converted to relative absorbed dose using background subtraction and normalization in a region of homogenous dose [9].

Two batches were prepared; i) four identical 500 ml circular gel phantoms (Ø 80 mm) and ii) three identical 1.3 liters circular gel phantoms (Ø 10 cm). For each batch, an identical un-irradiated gel phantom was used to acquire a background value. Gel vials irradiated to known doses were used to assure the linearity of the gel dose response.

2.2. Modulated arc treatment plans and delivery

To simulate tumour movement caused by respiratory motion, the gel phantoms were positioned on a programmable motion platform (Standard Imaging, Inc), which was set to carry out sinusoidal motion in the superior–inferior (SI) direction.

Two different RapidArc™ plans were delivered; i) A 6 MV lung plan was created in the Eclipse version 8.6 treatment planning system (TPS) using inverse optimisation and calculated with AAA. The plan was delivered using a Novalis TX™ linear accelerator (Varian Medical Systems) with a high definition MLC in one 358-degree arc rotation. The small target had a 4.86 cm³ volume and was irradiated with a planned target dose of 4 Gy using 790 MU. The collimator rotation was set to 45 degrees. The delivery was carried out both to a stationary gel phantom and to a gel phantom during motion with a peak-to-peak distance of 10 mm during a period of 4 s.

ii) A 18 MV prostate plan was created using a beta version of the pre-clinical RapidArc™ optimizer and calculated with the anisotropic analytical algorithm (AAA). The plan was delivered using a Clinac iX linear accelerator (Varian Medical Systems) in one arc rotation from 210 to 150°. The planned target dose was 3.3 Gy using 864 MU. The collimator rotation was set to 46 degrees. A dosimetric verification of this delivery using gel dosimetry and Monte Carlo calculation has earlier been published [8]. In this study the delivery was carried out again, both to a stationary gel phantom and to a phantom during motion with a peak-to-peak distance of 20 mm during a period of 5 s. Although the target volume in prostate plans doesn’t expect to be affected by a respiratory induced motion, this delivery was useful when investigating interplay effects.
2.3. Interplay effect definition
To be able to measure any potential dosimetric differences between the smoothing and interplay effect we take advantage of the very high spatial resolution in three dimensions that the polymer gel detector system provides.

In order to evaluate the dosimetric impact of the interplay between the phantom motion and the dynamic treatment delivery, we defined the dosimetric interplay effect as the relative 3D absorbed dose difference between the volumes obtained from the VMAT measurement during phantom motion and the VMAT measurement to a stationary phantom convolved with the motion function of the moving platform. The difference between the measured and convolved gel matrices was calculated as ((“during motion”−“convolved stationary”)/“convolved stationary”)*100. The motion function of the platform was a sinusoidal motion with an amplitude of 10 mm and a frequency of 4 s for the lung plan delivery (i) and with an amplitude of 20 mm and a frequency of 5 s for the prostate plan delivery (ii). Only the volume within the 90% isodose surface (approximating the target volume) was investigated.

If no relative absorbed dose deviations were detected, there would be no measurable interplay effects between the MLC motion and phantom motion, and the decreased high dose volume measured in the gel in motion would only depend on the smoothing effect.

To estimate the size of a detectable interplay effect, the observed dose difference was compared to the dose difference between two repeated stationary gel measurements for each delivery.

3. Results and discussion
The lung- and prostate VMAT plan deliveries were measured with a stationary gel phantom and with a phantom motion with amplitude of 10 mm and a frequency of 4 s, and amplitude of 20 mm amplitude and 5 s frequency, respectively. The total dosimetric effect of motion was evaluated, i.e. the dose difference between the volume obtained from the measurement during phantom motion and the measurement to a stationary phantom. The isodose volume ≥ 90% was investigated. The mean value and standard deviation of the differences obtained from the measurements were (-3.70±2.56)% with only 26.6% of the voxels within 2% dose difference for the lung plan (figure 1a) and (-4.31±4.80)% with only 32.6% of the voxels within 2% dose difference for the prostate plan (figure 1b).

![Figure 1](image-url)

**Figure 1:** The 90% isodose surface overlay of the gel measurements. The red volumes represent the stationary gel measurements and the green volumes represent the gel measurements obtained during motion. The overlay visualizes the relative absorbed dose reduction to target due to respiratory motion.

Investigating the interplay effect for the lung plan, the mean value and standard deviation of the relative dose difference between the measured VMAT delivery during phantom motion and the convolved stationary VMAT delivery resulted in (-1.2 ± 1.4)% with 71.2% of the voxels within 2% dose difference (figure 2a). This result was compared to the dose difference between two repeated stationary convolved gel measurement, which resulted in (0.064±0.51)% with 99.9% of the voxels within 2% dose difference and 94.2% of the voxels within 1% dose difference (figure 2b).
The corresponding interplay result for the prostate VMAT plan delivery was \((0.94 \pm 2.32)\%\) with 60.0\% of the voxels within 2\% dose difference. In this case, a repeated stationary measurement using a second gel batch had resulted in a relative dose difference of \((0.39\pm0.92)\%\) [8].

**Figure 2:** The distribution of voxel-by-voxel deviations between the different gel measurement sets within the volumes enclosed by the 90\% isodose surface for the lung VMAT plan delivery. The number of voxels is plotted against the difference in relative dose between the two analyzed volumes. Note the different scale of the ordinates. The interplay effect is presented in a) and the difference between repeated measurements in b).

### 4. Conclusions

The total dosimetric effect due to breathing motion and dynamic MLC motion during VMAT delivery resulted in an average of about 4\% target dose reduction. Comparing with the convolved stationary measurement, which includes only the smoothing effect, the average difference was decreased to around 1\%, and the remaining distribution was attributed to interplay effects. For repeated stationary measurement, i.e. without interplay effects but including all other measurements uncertainties (e.g. set-up), the differences had a narrow distribution with a standard deviation between 0.5-0.9\% (1SD). Thus, the larger standard deviations of 1.4\% (1SD) in the lung plan case (with a motion of 1 cm amplitude and 4 s frequency) and 2.3\% (1SD) in the prostate plan case (2 cm amplitude and 5 s frequency), were interpreted as interplay effects.

### 5. References

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