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Forcing lateral electron disequilibrium to spare lung tissue: a novel technique for stereotactic body radiation therapy of lung cancer

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Abstract
Stereotactic body radiation therapy (SBRT) has quickly become a preferred treatment option for early-stage lung cancer patients who are ineligible for surgery. This technique uses tightly conformed megavoltage (MV) x-ray beams to irradiate a tumour with ablative doses in only a few treatment fractions. Small high energy x-ray fields can cause lateral electron disequilibrium (LED) to occur within low density media, which can reduce tumour dose. These dose effects may be challenging to predict using analytic dose calculation algorithms, especially at higher beam energies. As a result, previous authors have suggested using low energy photons (<10 MV) and larger fields (>5 × 5 cm\textsuperscript{2}) for lung cancer patients to avoid the negative dosimetric effects of LED. In this work, we propose a new form of SBRT, described as LED-optimized SBRT (LED-SBRT), which utilizes radiotherapy (RT) parameters designed to cause LED to advantage. It will be shown that LED-SBRT creates enhanced dose gradients at the tumour/lung interface, which can be used to manipulate tumour dose, and/or normal lung dose. To demonstrate the potential benefits of LED-SBRT, the DOSXYZnrc (National Research Council of Canada, Ottawa, ON) Monte Carlo (MC) software was used to calculate dose within a cylindrical phantom and a typical lung patient. 6 MV or 18 MV x-ray fields were focused onto a small tumour volume (diameter ~1 cm). For the phantom, square fields of 1 × 1 cm\textsuperscript{2}, 3 × 3 cm\textsuperscript{2}, or 5 × 5 cm\textsuperscript{2} were applied. However, in the patient, 3 × 1 cm\textsuperscript{2}, 3 × 2 cm\textsuperscript{2}, 3 × 2.5 cm\textsuperscript{2}, or 3 × 3 cm\textsuperscript{2} field sizes were used in simulations to assure target coverage in the superior–inferior direction.

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To mimic a 180° SBRT arc in the (symmetric) phantom, a single beam profile was calculated, rotated, and beams were summed at 1° segments to accumulate an arc dose distribution. For the patient, a 360° arc was modelled with 36 equally weighted (and spaced) fields focused on the tumour centre. A planning target volume (PTV) was generated by considering the extent of tumour motion over the patient’s breathing cycle and set-up uncertainties. All patient dose results were normalized such that at least 95% of the PTV received at least 54 Gy (i.e. D95 = 54 Gy). Further, we introduce ‘LED maps’ as a novel clinical tool to compare the magnitude of LED resulting from the various SBRT arc plans. Results from the phantom simulation suggest that the best lung sparing occurred for RT parameters that cause severe LED. For equal tumour dose coverage, normal lung dose (2 cm outside the target region) was reduced from 92% to 23%, comparing results between the 18 MV (5 × 5 cm²) and 18 MV (1 × 1 cm²) arc simulations. In addition to reduced lung dose for the 18 MV (1 × 1 cm²) arc, maximal tumour dose increased beyond 125%. Thus, LED can create steep dose gradients to spare normal lung, while increasing tumour dose levels (if desired). In the patient simulation, a LED-optimized arc plan was designed using either 18 MV (3 × 1 cm²) or 6 MV (3 × 3 cm²) beams. Both plans met the D95 dose coverage requirement for the target. However, the LED-optimized plan increased the maximum, mean, and minimum dose within the PTV by as much as 80 Gy, 11 Gy, and 3 Gy, respectively. Despite increased tumour dose levels, the 18 MV (3 × 1 cm²) arc plan improved or maintained the V20, V5, and mean lung dose metrics compared to the 6 MV (3 × 3 cm²) simulation. We conclude that LED-SBRT has the potential to increase dose gradients, and dose levels within a small lung tumour. The magnitude of tumour dose increase or lung sparing can be optimized through manipulation of RT parameters (e.g. beam energy and field size).

(Some figures may appear in colour only in the online journal)

1. Introduction

Non-small-cell lung cancer continues to be a leading cause of cancer related death in North America (Siegel et al 2011). The number of lung cancer patients being diagnosed with early-staged disease (i.e. stage I or II) has grown due to the increased availability of computed tomography (CT) imaging (Henschke et al 2006). For these patients, the preferable treatment option is surgical lung resection. However, comorbidities, such as emphysema and heart disease, can make surgery intolerable (Timmerman et al 2010). An alternative form of treatment for these patients is conventional radiation therapy (RT) (delivered in 20–30 fractions), where a homogeneous dose is delivered to the target. Unfortunately, this technique results in poor tumour control probabilities (TCPs) of 30%–40% (Timmerman et al 2010), and a five year survival rate of 20% (Wisnivesky et al 2005). A recently developed RT technique, known as stereotactic body radiation therapy (SBRT) or stereotactic ablative radiotherapy, has been shown to improve TCP to greater than 90% and survival rates up to 40% at three years (Heinzerling et al 2011). The SBRT technique uses image guidance (Bissonnette et al 2009, Otto 2008) to accurately focus multiple, small megavoltage (MV) radiation beams onto a tumour volume, delivering ablative doses (e.g. 54 Gy) in only a few treatment fractions (e.g. 1–5 sessions) (Timmerman et al 2007). In contrast to conventional RT, SBRT uses steep dose
Forcing LED to spare lung tissue for lung SBRT

Healthy lung tissue can range in density from 0.1 to 0.4 g cm\(^{-3}\) (Rosenblum et al 1980, Van Dyk et al 1982). In contrast, for lung cancer patients also afflicted by emphysema (Wilson et al 2008), lung densities can be lower than 0.1 g cm\(^{-3}\) (Washko et al 2011). The dose distribution in low density media is affected by two opposing effects: (1) increased primary photon transmission, and (2) amplified secondary electron range. For conditions of charged particle equilibrium (CPE), enhanced photon transmission (effect 1) dominates the lung dose distribution, which increases the dose within lung and tumour (compared to a homogeneous water medium) (Yorke et al 1996). In contrast, for conditions that disrupt electron equilibrium (effect 2), large reductions of dose within lung and tumour tissues are possible (Disher et al 2012, Metcalfe et al 1993, Aarup et al 2009, Carrasco et al 2004, Mackie et al 1985). Lateral electron disequilibrium (LED) also significantly expands the dose penumbra at the field edge, which may result in inadequate target coverage at the field periphery (Ekstrand and Barnes 1990, Kornelsen and Young 1982).


For radiotherapeutic conditions that disrupt equilibrium (>4 MV photons, field sizes <5 \times 5\text{cm}^2, lung density <0.4 g cm\(^{-3}\)), the Monte Carlo (MC) technique (Ahnesjö and Aspradakis 1999) is the preferred method for determining accurate dose distributions. In contrast to analytical methods (Ahnesjö et al 1987 and Tillikainen et al 2008), MC methods explicitly track electron transport, and have been used to benchmark simpler dose calculation algorithms (Aarup et al 2009, Fogliata et al 2007, Hasenbalg et al 2007, Panettieri et al 2007, Sterpin et al 2007, Chow et al 2009, Jones and Das 2005, Carrasco et al 2004). Previously, our group used the MC technique to determine the specific combination of radiation therapy parameters that result in LED (Disher et al 2012). In a phantom study, a small tumour (1 \times 1 \times 1\text{cm}^3) was embedded within lung tissue, and irradiated using a single 18 MV (3 \times 3\text{cm}^2) field. Under conditions of severe LED, lung and tumour depth dose were reduced by as much as 80% and 15% (with respect to an all water absorber), respectively. These results imply that LED could be exploited to leverage a therapeutic ratio that maximizes the dose within the tumour, while controlling healthy lung dose to acceptable levels. Blomquist et al were the first to propose that LED could be used to safely increase the dose delivered to lung tumours (Blomquist and Karlsson 1998, Blomquist et al 2002). They proposed using 50 MV radiation fields (e.g. 2), and a traditional dose fractionation scheme (e.g. 30 fractions). However, such a technique is not clinically viable.

In this work, we propose a novel LED-optimized SBRT (LED-SBRT) treatment method, where specific radiotherapeutic parameters are chosen in order to cause extreme LED. This will be demonstrated with the introduction of a new clinical ‘tool’ described as LED maps. Further, using both a lung phantom and patient MC simulation, it will be shown that LED-SBRT can be used to enhance the steepness of dose gradients, to additionally increase the ablative levels of dose within the tumour, and further reduce the dose in normal lung. The LED-SBRT technique
provides an opportunity to optimize the desired tumour dose enhancement and/or lung tissue sparing via manipulation of RT parameters (beam energy and field size) for a given tumour size. With LED-SBRT, there is an opportunity to increase tumour dose. However, this may be perceived as controversial to the community, and a discussion on this topic is provided here-in.

2. Materials and methods

2.1. Monte Carlo codes and parameters

MC simulations were performed using the DOSXYZnrc user code (National Research Council of Canada, Ottawa, ON). Simulations were run concurrently using a cluster of PC-based 60 independent Intel Xeon central processing units (Intel Corporation, Santa Carla, CA). These systems operated at processing speeds of 2.67 or 3.4 GHz, and had a combined accessible total RAM of 102 GB. For lung phantom simulations, electron and photon transport parameters (i.e. ECUT and PCUT) were set as ECUT = 0.521 MeV, and PCUT = 0.010 MeV. For the lung patient simulation, ECUT was varied between 0.521 MeV, 6 MeV, or 18 MeV energies, and PCUT = 0.010 MeV. For electron energies below ECUT, DOSXYZnrc terminates the history and deposits the electron energy ‘on the spot’ (Ma et al 1995). Setting ECUT to the maximal photon energy will result in all liberated electrons being absorbed locally or at the site of photon interaction. This is analogous to simulating CPE, and the calculated dose is unaffected by electron transport. By setting ECUT as low as possible (i.e. 0.521 MeV (including rest mass energy)) the dose is dependent on electron scattering conditions, and CPE or LED maybe observed. Finally, PRESTA II (Kawrakow 2000) and EXACT algorithms were selected as the electron step and boundary crossing algorithms. DOSXYZnrc was used to perform all dose calculations, and up to $8 \times 10^9$ histories were used per simulation to keep statistical noise to less than 2% for dose voxels. The depth–dose profiles displayed in subsequent figures were normalized to the dose at maximum depth (i.e. $D_{\text{max}}$ per energy and field size) in water unless specified otherwise.

The suitability of DOSXYZnrc to accurately calculate the dose distribution for conditions of extreme LED has been assessed previously by our group (Disher et al 2012). In brief, a real water–air–water phantom was created at our centre, which was also virtually modelled within the DOSXYZnrc software. We observed better than 2% agreement comparing measurement against MC dose calculation within water regions. Similarly in air regions, where severe LED persists, measurement and calculation agreed within 3%. An analogous MC validation study was performed by Chow et al (2009), which produced results comparable to our own.

2.2. Cylindrical lung phantom simulations

MicroView Analysis+ software V2.2 (GE Healthcare®, Waukesha, WI) was used to create a virtual CT image of a cylindrical lung phantom (see figures 1(a) and (b)). This phantom was used to demonstrate the potential tumour/lung dose effects of LED-SBRT under the assumptions of homogeneous lung density, and in the absence of lung breathing motion. The height and diameter of the phantom were 25 cm. At the phantom centre, a 1 cm solid water cylindrical tumour (density = 1 g cm$^{-3}$) was embedded into an inner cylindrical lung shell (density = 0.25 g cm$^{-3}$), which had annuli extending from $r = 0.5–7.5$ cm, and a height equal to 25 cm ($z = -12.5$ cm to 12.5 cm). The outer-most ‘chest wall’ shell consisted of water (density = 1 g cm$^{-3}$) annuli traversing $r = 7.5$ cm to 12.5 cm in addition to having a height equal to 25 cm ($z = -12.5$ cm to 12.5 cm). The CTCREATE module (Ma et al 1995) was
Figure 1. (a) Shows a schematic diagram (not to scale) of the cylindrical phantom used in this work. (b) Displays the transverse view of the phantom at the tumour centre. The tumour was modelled by a small water cylinder with a height and diameter of 1 cm. (c) Shows the transverse view of the lung patient including tumour (spherical diameter $\sim$1 cm). To demonstrate the lung sparing effect of LED, 6 or 18 MV beam energies (various field sizes) were focused onto the tumour centre in both phantom and patient MC simulations.

used to convert the CT image of the phantom into a DOSXYZnrc-compatible form (i.e. an egphant file) with $1 \times 1 \times 3$ mm$^3$ sized voxels.

Source type '0' was selected within the input settings, and 6 and 18 MV photon spectra (Mohan et al 1985) were applied. For each energy, square field sizes of $1 \times 1$ cm$^2$, $3 \times 3$ cm$^2$, and $5 \times 5$ cm$^2$ were used to collimate the photon field. To simulate a 180° SBRT arc, a single field dose distribution was calculated at 0°. This dose distribution was then exported into Matlab V. R2012a (The MathWorks Inc., Natick, MA) software where it was rotated and summed incrementally by 1° segments until the total cumulative 180° arc dose was complete. This approach was valid as the phantom is symmetric and homogeneous in composition.
2.3. Lung patient simulations

A CT image of a SBRT lung cancer patient was acquired using a 16-slice helical CT simulator unit (Brilliance Big Bore CT, Philips Medical Systems, USA). Image acquisition parameters were set to: 120 kVp, 400 mAs/slice, 0.5 s rotation time, and the pitch varied in accordance with the patient’s breathing cycle. CT images were reconstructed at ten different points within the breathing cycle, and a time-averaged four-dimensional CT (4DCT) was created for use in this study. The 4DCT image set was reconstructed using a slice thickness of 3 mm, onto a $512 \times 512$ pixel matrix over a field-of-view of 45 cm (see figure 1(c)). CTCREATE was again used to convert the lung patient CT data to the ‘egsphant’ format with a voxel resolution of approximately equal to $1 \times 1 \times 3$ mm$^3$.

As the lung cancer patient was originally treated with the SBRT technique at our centre, lung and tumour contours were generated by a radiation oncologist. The patient’s lung tumour was spherically shaped with a diameter of $\sim 1$ cm. Ten separate gross tumour volume (GTV) contours were created to encompass the extent of the tumour motion for each phase of the patient’s breathing cycle (tumour motion occurred primarily along the superior–inferior direction). The internal gross tumour volume (IGTV) was created by taking the union of each GTV over the entire breathing cycle. The planning target volume (PTV) included the IGTV plus a 5 mm isotropic expansion to account for treatment uncertainties (i.e. patient set-up). The PTV was ovoid shaped with a length of $\sim 3$ cm along the superior-to-inferior direction, and a diameter of $\sim 1.5$ cm in the transverse plane. As well, a healthy lung volume was determined by considering the patient’s entire lung volume less the IGTV. Dose calculations were performed within DOSXYZnrc by aiming either 6 or 18 MV photon beams (Mohan et al 1985) onto the patient’s tumour centre. Source type ‘1’ was selected within the input settings for the patient MC simulations. This allowed for angular rotation of the photon source about the patient’s superior–inferior axis. The field size was chosen to be as small as possible while still providing adequate longitudinal coverage to the PTV. Variations in field size were therefore only possible along the transverse axis.

Since LED is more prevalent at higher beam energies we varied the square field size for the 18 MV energy only ($3 \times 3$ cm$^2$, $3 \times 2.5$ cm$^2$, $3 \times 2$ cm$^2$, and $3 \times 1$ cm$^2$). Clinical SBRT lung recommendations (Radiation Therapy Oncology Group (RTOG) trials 0236, 0618, 1021, 0813, and 0915) suggest using beam energies less than 10 MV. Thus, the 6 MV ($3 \times 3$ cm$^2$) simulation was selected to represent the clinical control for comparison. For each combination of beam energy and field size, 36 equally spaced and weighted fields were used to span a range of 360$^\circ$ to simulate an SBRT arc treatment. All arc dose distributions were normalized such that 95% or more of the PTV received at least 54 Gy (i.e. the D95 dose prescription requirement). Finally, the normalized dose distributions, contours, and CT data were analyzed using the CERR software run within Matlab (Deasy et al 2003).

2.4. Lateral electron disequilibrium maps

An excellent review of the relevant physics involving MV photons and low density media has been provided by The American Associate of Physicists in Medicine (AAPM) Report Number 85 (Papanikolaou et al 2004). In short, energy deposition in human tissues (due to impinging photon fluence) can be broken into two sequential components: (1) photon interactions that impart kinetic energy to electrons, and (2) electrons depositing energy locally through ionization and excitation events along their path. From step (1), we define KERMA as the kinetic energy released to electrons per unit mass; from step (2), KERMAC is the kinetic energy released and absorbed locally along electron paths per unit mass (KERMAC is...
equal to KERMA less radiative Bremsstrahlung events). CPE exists when there is a balance between the electron energy fluence entering and leaving a small volume of interest. For CPE conditions, the absorbed dose \( D \) is equal to KERMA \( K_c \):

\[
D = K_c.
\]  

(1)

However, true CPE is impossible in a clinical radiotherapy beam because photon beam divergence and attenuation perturb the ‘steady state’ flux of electrons (Johns and Cunningham 1983). Conversely, transient CPE (TCPE) is achievable along the central-axis of a field of radiation, so long as the depth exceeds the maximum forward electron range, and the field radius surpasses the lateral electron range (establishing lateral electron equilibrium). Under TCPE the dose scales proportionally to KERMA \( K_c \) such that their ratio is always greater than unity at depths greater than \( D_{\text{max}} \):

\[
\frac{D}{K_c} > 1.
\]  

(2)

The primary goal of this paper was to select appropriate radiotherapeutic parameters that force LED within lung tissue such that the ratio in equation (2) is advantageously less than unity:

\[
\frac{D}{K_c} < 1.
\]  

(3)

As such, it may be possible to spare lung tissue from the effects of radiation exposure along beam path directions. Finally, by considering \( D/K_c \), we can determine how electron trajectories affect the overall dose distribution and have an index of disequilibrium. Visualizations of this ratio can provide a map of LED.

3. Results

3.1. Cylindrical lung phantom simulations

Figure 2(a) displays a transverse slice of the cylindrical lung phantom at the tumour centre. The red line depicts where single field dose profiles were extracted. Figure 2(b) shows the central-axis depth–dose profile for a 6 MV beam energy collimated to \( 1 \times 1 \text{ cm}^2 \), \( 3 \times 3 \text{ cm}^2 \) or \( 5 \times 5 \text{ cm}^2 \) field sizes. For the 6 MV \( (5 \times 5 \text{ cm}^2) \) profile, the dose within the downstream lung, tumour and water shell was maintained due to reduced photon attenuation through the low density lung tissue. On the contrary, the 6 MV \( (3 \times 3 \text{ cm}^2) \) and 6 MV \( (1 \times 1 \text{ cm}^2) \) dose profiles both showed reduced dose levels within the lung shell as equilibrium was lost for this selection of RT parameters. As a general rule, the lateral path-length of free electrons is \( \sim 1/3–1/2 \) the longitudinal electron range (Mackie et al. 1985). In water, for a 6 MV photon source \( (D_{\text{max}} = 1.5 \text{ cm}) \), the lateral range of electrons was between 0.5 and 0.75 cm. However, since the electron path-length scales inversely with density, the lateral range increased from 2 cm up to 3 cm in lung tissue. As such, the lateral electron trajectory could reach the lateral beam radius (1.5 cm). These electrons scattered beyond the field edge, were not replaced, which reduced the central-axis depth–dose profile within lung tissues (Mackie et al. 1985, Papanikolaou et al. 2004, Chow et al. 2009). Also note that LED was more severe using the \( 1 \times 1 \text{ cm}^2 \) field size, which produced the lowest dose levels within lung tissue. Despite the ‘build-down’ of dose within lung tissues, there was still a ‘build-up’ of dose within the tumour.

Figure 2(c) shows comparable results for the 18 MV beam. Also notice that \( D_{\text{max}} \) appeared to be slightly more shallow for the 18 MV \( (1 \times 1 \text{ cm}^2) \) result in comparison to the other profiles. As the field size was decreased below the lateral electron range in water, Compton electrons liberated from the field periphery no longer reach the central-axis at depths below
(a) A transverse view of the phantom (at the tumour center) displaying the location of the depth dose profile (i.e. the red line), and the single field of radiation.

(b) Single field depth-dose profiles acquired from 6 MV simulations.

Figure 2. (a) Shows a transverse view of the cylindrical phantom (at the tumour centre) including the line profile where single field depth–dose profiles were acquired for a 6 MV (b) and 18 MV (c) beam energy. Note that LED is more dominate at higher beam energies and smaller field sizes.

Figure 3(a) displays a transverse slice of the cylindrical lung phantom at the tumour centre. The red line depicts where 180° arc dose profiles were extracted. Figures 3(b) and (c) display arc depth–dose profiles for 6 and 18 MV beam energies for various field sizes (1 × 1 cm², 3 × 3 cm² or 5 × 5 cm²). Results were normalized such that 100% depth dose falls on the tumour edge. In this way, changes in lung and tumour dose can be better visualized for equal dose coverage of the tumour. In both figures, shrinking the field size exaggerated LED, which
greatly spared the lung tissue. For example, in figure 3(c), the lung dose at depth = 10.5 cm decreased from 92% to 62% or 23% for the 5 × 5 cm², 3 × 3 cm² or 1 × 1 cm² fields (18 MV energy). In both figures 3(b) and (c), despite reduced lung dose levels, the maximal tumour dose was greater than 125% for the 1 × 1 cm² field size (6 and 18 MV energy). These dosimetric effects are due to the enhanced dose gradients present at the lung/tumour interface, which occur when LED is severe.

3.2. Lung patient simulations

Figure 4(a) shows a transverse view of a lung patient at the tumour centre. The red line indicates where arc depth–dose comparisons were made in figure 4(d). Figures 4(b) and (c) display the clinical standard (6 MV (3 × 3 cm²)) and LED-optimized (18 MV (3 × 1 cm²)) 360° arc dose distributions overlaid on the lung patient anatomy. Comparing figures 4(b) and (c), the reduction in field size along the transverse plane is easily visualized. Further, the high dose and steep dose gradient regions are better confined to the vicinity of tumour in figure 4(c). Also notice the low to medium dose region within the right lung (light green and yellow colours) that encompasses a smaller area in figure 4(c). Figure 4(d) compares the 6 MV (3 × 3 cm²) arc to the various sized arcs at 18 MV energy. The magnitude of lung sparing and tumour dose increase was related to the extent of LED. For example, the lung dose at depth = 12 cm was 22 Gy, 24 Gy, 26 Gy, and 29 Gy for the 18 MV 3 × 1 cm², 3 × 2 cm², 3 × 2.5 cm², or 3 × 3 cm² compared to 28 Gy for the 6 MV (3 × 3 cm²) plan. The greatest lung sparing occurred using the highest energy beam collimated to the smallest field size. Also, tumour dose was increased to a greater extent for arc plans where LED was more severe. Table 1 displays the maximal, mean, and minimum dose metrics for the PTV across the various arc plans. For example, comparing the LED-optimized plan (18 MV (3 × 1 cm²)) to the conventional arc (6 MV (3 × 3 cm²)), the maximal, mean, and minimal dose were increased by 80 Gy, 11 Gy, and 3 Gy, respectively. These results indicate that LED can be exploited to create steep dose
Figure 3. (a) Shows a transverse view of the cylindrical phantom (at the tumour centre) including the line profile where arc depth dose profiles were acquired for 6 MV (b) and 18 MV (c) beam energies. Note that LED, established for 18 MV (1 $\times$ 1 cm$^2$) energies, reduced lung dose by as much as 70%.

(b) 180° arc depth-dose profiles acquired from 6 MV simulations.

Figure 5(a) shows a coronal view of the lung patient at the tumour centre. The red line indicates where arc depth–dose comparisons were made in figure 5(d). Figures 5(b) and (c) display the clinical standard (6 MV (3 $\times$ 3 cm$^2$)) and LED-optimized (18 MV (3 $\times$ 1 cm$^2$)) 360° arc dose distributions overlaid on the lung patient anatomy. As the PTV’s longest axis
Figure 3. (Continued.)

Figure 4. (a) Shows a transverse view of the lung patient including the line profile where arc depth–dose profiles were acquired. (b) and (c) display a transverse view of the 6 MV ($3 \times 3$ cm$^2$) and 18 MV ($3 \times 1$ cm$^2$) $360^\circ$ arc dose distributions in the vicinity of the tumour. (d) presents various $360^\circ$ arc depth–dose profiles. The LED-optimized arc (i.e. 18 MV ($3 \times 1$ cm$^2$)) produced a ‘hot spot’ in the tumour centre that was approximately two times the value observed using the clinical standard arc (i.e. 6 MV ($3 \times 3$ cm$^2$)). Despite increased tumour dose levels, the LED-optimized plan produced the lowest lung dose distribution.
Figure 5. (a) Shows a coronal view of the lung patient including the line profile where arc depth-dose profiles were acquired. (b) and (c) display a coronal view of the 6 MV (3 × 3 cm²) and 18 MV (3 × 1 cm²) 360° arc dose distributions in the vicinity of the tumour. (d) presents various 360° arc depth dose profiles. Comparing the LED-optimized arc (i.e. 18 MV (3 × 1 cm²)) to the clinical standard arc (i.e. 6 MV (3 × 3 cm²)), the PTV received more dose along the superior–inferior axis.

Table 1. Compares the mean, maximum, and minimum dose values within the PTV for the various arc plans. The LED-optimized plan (18 MV (3 × 1 cm²)) produced the highest dose values for all three PTV dose metrics.

<table>
<thead>
<tr>
<th>PTV dose metrics</th>
<th>6 MV 3 × 3 cm²</th>
<th>18 MV 3 × 1 cm²</th>
<th>18 MV 3 × 2 cm²</th>
<th>18 MV 3 × 2.5 cm²</th>
<th>18 MV 3 × 3 cm²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean dose (Gy)</td>
<td>70</td>
<td>81</td>
<td>72</td>
<td>70</td>
<td>70</td>
</tr>
<tr>
<td>Max. dose (Gy)</td>
<td>89</td>
<td>169</td>
<td>105</td>
<td>96</td>
<td>91</td>
</tr>
<tr>
<td>Min. dose (Gy)</td>
<td>44</td>
<td>47</td>
<td>45</td>
<td>44</td>
<td>44</td>
</tr>
</tbody>
</table>

aligned with the superior-to-inferior direction, it was not possible to reduce the field size in the coronal plane while maintaining adequate PTV coverage. Also, comparing figures 5(b) and (c), the dose penumbra was wider for the LED-optimized plan, an effect due to the increased lateral electron range for higher energy electrons. This is also evident from observing figure 5(d) as the dose profile just beyond the PTV border is the highest for the LED-optimized plan. As in figure 4(d), the coronal dose profile within the PTV was largest for the 18 MV (3 × 1 cm²) arc, followed by the 18 MV (3 × 2 cm²), 18 MV (3 × 2.5 cm²), 18 MV (3 × 3 cm²), and 6 MV (3 × 3 cm²) plans (see table 1 for specific dose values within the PTV).

Figure 6 compares the dose volume histograms (DVH) for the PTV for the 18 MV (3 × 1 cm²), 18 MV (3 × 2 cm²), 18 MV (3 × 2.5 cm²), 18 MV (3 × 3 cm²), and 6 MV (3 × 3 cm²) arc plans. All plans met the prescription requirement such that 95% or more of the
Figure 6. Displays the DVHs comparing arc dose for the PTV using either the 6 MV \(3 \times 3\) cm\(^2\), 18 MV \(3 \times 3\) cm\(^2\), 18 MV \(3 \times 2.5\) cm\(^2\), 18 MV \(3 \times 2\) cm\(^2\), or 18 MV \(3 \times 1\) cm\(^2\) plans. All plans met the D95 prescription requirement. In addition, the LED-optimized plan (i.e. 18 MV \(3 \times 1\) cm\(^2\)) produced a ‘hotspot’ of approximately 170 Gy at the tumour centre (∼3 times the prescription dose of 54 Gy).

Table 2. Compares three lung dose metrics for the various arc plans. Mean dose = average dose from the entire volume of healthy lung tissue (lung volume less the IGTV). V20 = the per cent of the healthy lung volume receiving 20 Gy or more. V5 = the per cent of the healthy lung volume receiving 5 Gy or more. Both the V20 and mean dose metrics are lowest for the LED-optimized, 18 MV \(3 \times 1\) cm\(^2\), plan.

<table>
<thead>
<tr>
<th>Lung metrics</th>
<th>6 MV (3 \times 3) cm(^2)</th>
<th>18 MV (3 \times 3) cm(^2)</th>
<th>18 MV (3 \times 1) cm(^2)</th>
<th>18 MV (3 \times 2) cm(^2)</th>
<th>18 MV (3 \times 2.5) cm(^2)</th>
<th>18 MV (3 \times 3) cm(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean dose</td>
<td>3.7 Gy</td>
<td>3.4 Gy</td>
<td>3.6 Gy</td>
<td>3.9 Gy</td>
<td>4.2 Gy</td>
<td></td>
</tr>
<tr>
<td>V20</td>
<td>4.3%</td>
<td>3.2%</td>
<td>3.6%</td>
<td>4.1%</td>
<td>5.0%</td>
<td></td>
</tr>
<tr>
<td>V5</td>
<td>18%</td>
<td>18%</td>
<td>20%</td>
<td>22%</td>
<td>24%</td>
<td></td>
</tr>
</tbody>
</table>

PTV received at least 54 Gy (i.e. D95). However, plans that exploited the LED phenomenon produced a significant ‘hot spot’ within the PTV centre (see maximum dose in table 1).

Figure 7 displays DVHs with regard to the healthy lung volume and the various arc plans. Upon first inspection of figure 7(a), there appeared to be very little difference between the lung DVHs across all plans. However, figure 7(b) shows an expanded view of the DHVs, and in general, the lung DVHs increase in order starting from the 18 MV \(3 \times 1\) cm\(^2\) plan, up to 18 MV \(3 \times 2\) cm\(^2\), 18 MV \(3 \times 2.5\) cm\(^2\), 6 MV \(3 \times 3\) cm\(^2\), and 18 MV \(3 \times 3\) cm\(^2\) plans. Note there were some deviations away from this trend in the vicinity of the V5 region where the 6 MV \(3 \times 3\) cm\(^2\) and 18 MV \(3 \times 1\) cm\(^2\) arcs were comparable, but lower than for the remaining plans. The specific variations in the V5, V20, and mean lung dose are provided in table 2. Of noticeable importance is the sensitivity of these lung dose metrics to changes in the radiotherapeutic parameters. For example, by increasing the 18 MV transverse field size
(a) Dose volume histogram for healthy lung

(b) Expanded view of dose volume histogram for healthy lung

Figure 7. (a) Displays the DVHs comparing arc dose for the healthy lung volume (lung volume less the IGTV) using either the 6 MV $3 \times 3 \text{cm}^2$, 18 MV $3 \times 3 \text{cm}^2$, 18 MV $3 \times 2.5 \text{cm}^2$, or 18 MV $3 \times 1 \text{cm}^2$ plans. (b) displays the same information, but expands on the V5 and V20 regions (i.e. the volume of healthy lung receiving 5 Gy or 20 Gy or more). Note the lung DVH related to the 18 MV $3 \times 1 \text{cm}^2$ plan received the least dose in the V20 region. See table 2 for a comparison of lung dose metrics.

From 1 cm to 3 cm, we observed changes in the mean lung dose, V20, and V5 of 0.8 Gy, 1.8%, and 6%, respectively. Finally, comparing the lung dose metrics of the LED-optimized arc (18 MV $3 \times 1 \text{cm}^2$) to our clinical standard (6 MV $3 \times 3 \text{cm}^2$), the V20 and mean lung dose were lower while the V5 remained the same. Indeed, careful attention must be paid to these parameters if we are to improve or maintain the normal lung dose distribution, while intentionally manipulating the extent of LED.

3.3. Lateral electron disequilibrium maps

By studying the dose to KERMA ratio we can determine whether the chosen RT parameters (i.e. photon energy, field size, and lung density) combine to promote LED (dose/KERMA < 1). As a demonstration, we focused a single 6 MV $10 \times 10 \text{cm}^2$ field of radiation onto the
Forcing LED to spare lung tissue for lung SBRT. We then repeated this process using a single field of radiation utilizing the proposed LED-optimized RT parameters (i.e. 18 MV (3 × 1 cm²)). Figure 8(a) shows the transverse view of the lung patient with the 6 MV (10 × 10 cm²) field demarked in red, and the 18 MV (3 × 1 cm²) field demarked in blue. In figure 8(b) the KERMA and dose for the 6 MV (10 × 10 cm²) field are plotted along the central-axis of the beam. Initially, within the patient’s anterior chest wall, the dose is well below the KERMA. However, beyond D_max the KERMA and dose values converge. For shallow depths above D_max, longitudinal electron disequilibrium exists, which creates the characteristic build-up curve within the anterior chest wall. For depths below D_max, the dose is similar to the KERMA within the chest wall, tumour, and lung tissues. Since the 10 × 10 cm² field size is large enough to establish lateral electron equilibrium, the conditions for TCPE are met, and dose is maintained throughout these tissues.

Figure 8(c) shows a similar comparison using the 18 MV (3 × 1 cm²) settings. For a 3 × 1 cm² field size, with the shortest axis aligned along the transverse plane, lateral electron equilibrium was not achievable for water density. Therefore, the dose was less than the KERMA over the entire profile. The largest reductions in the dose profile occurred within lung tissue, as low densities exaggerated LED and enhanced lung sparing. Also, there was an observed dose ‘rebuild-up’ within the tumour despite the lower lung dose.

Figures 9(a)–(e) display a transverse slice of the dose-to-KERMA ratios (or LED maps) for the 6 MV (3 × 3 cm²), 18 MV (3 × 3 cm²), 18 MV (3 × 2.5 cm²), 18 MV (3 × 2 cm²), and 18 MV (3 × 1 cm²) arc plans. For increased beam energy and smaller field sizes, the ratio was reduced below unity (an indicator of LED). On the contrary, for lower energy and larger field sizes, the ratio approached unity. For example, the 18 MV (3 × 1 cm²) LED map contained many lung regions valued from 0.4 to 0.6, while the 6 MV (3 × 3 cm²) map displayed values between 0.6 and 1.0. Figure 9(f) shows the LED volume histograms (LVHs) for the various arc plans. These histograms were created by considering only those lung voxels contained within the beam paths (the entire healthy lung volume was not considered in this analysis). Once again, for the volume of lung tissue traversed by the arcs, the lowest dose to KERMA ratios were observed for those plans with the highest energy and smallest field size (i.e. 18 MV (3 × 1 cm²) or LED-optimized plan). These findings explain the results shown in figures 4–7, and support the hypothesis that the LED phenomenon can be exploited to maintain or lower lung dose, while increasing dose levels within the tumour volume. Finally, the ripple artefact observed between adjacent fields in figures 9(a)–(e), and discontinuities present within figure 9(g), are due to an under-sampled arc dose distribution. We expect these artefacts to greatly diminish with the addition of more overlapping fields to complete a full 360° SBRT arc.

4. Discussion

4.1. LED-SBRT: potential benefits and controversy

The LED-SBRT technique uses specific combinations of beam energy and field size in order to intentionally disrupt CPE in lung tissue, thus forcing LED. In doing so, an extremely steep dose gradient at the tumour/lung interface occurs, which can be used to increase dose within the tumour, and/or maintain or lower dose in normal lung. The magnitude of the dose gradient spanning these tissues depends on the selected RT and patient parameters (e.g. lung density). Thus, in the planning of LED-SBRT, a physicist must be aware of the dose balance between adjacent tumour and lung tissues, and carefully design treatment in accordance with SBRT protocols (Hurkmans et al 2009).
(a) Transverse view of lung patient CT with the single field edges demarked (red and blue)

(b) Comparison of KERMA and dose for a 6 MV 10×10 cm² single field

(c) Comparison of KERMA and dose for an 18 MV 3×1 cm² single field

Figure 8. (a) Shows a transverse view of the lung patient with the 6 MV (10 × 10 cm²) and 18 MV (3 × 1 cm²) field edges demarked in red and blue. (b) and (c) compare the KERMA (ECUT = 6 MeV or 18 MeV) to dose (ECUT = 0.521 MeV) along the field central-axis. In (c), LED causes the KERMA and dose profiles to diverge. This effect can be exploited to spare lung tissue for SBRT of lung cancer.
Forcing LED to spare lung tissue for lung SBRT

Figures 9. (a)–(e) Displays the ratio of dose to KERMA, which indicates the severity of LED for each arc plan. As the ratio decreases to zero, LED is more prevalent, which spares lung tissue along beam path directions. (f) Shows LED volume histograms (LVH) acquired from the various arc plans. The LVHs were acquired from the volume of healthy tissue along beam path directions only (not the entire healthy lung volume). The LVH for the 18 MV $3 \times 1$ cm$^2$ demonstrates that LED is most prevalent for this choice of beam energy and field size.

Using LED-SBRT for our sample patient, we were able to increase the minimum, mean, and maximum dose found within the PTV, while maintaining PTV dose coverage and lung dose. The hypothetical benefit of increasing tumour dose for early-stage lung cancer may include: higher tumour control, lower probability of local tumour recurrence, improved radiobiological effects (tumour hypoxia), and hence better overall survival rates. Simultaneously, the benefit associated with a lower lung dose can potentially reduce side-effects, such as radiation pneumonitis and fibrosis. However, the therapeutic benefits associated with LED-SBRT will be limited in clinical practice, depending upon the location of the tumour within lung. For example, in our sample patient, the tumour was surrounded by sufficient lung tissue to force LED. In contrast, tumours located adjacent to chest wall or mediastinum will become difficult to intentionally establish LED, due to surrounding water equivalent material. Nonetheless, under the latter scenario, our technique may still be beneficial if some LED can be produced, thereby creating a steeper dose gradient to spare adjacent critical structures (e.g. ribs, bronchus, trachea, and esophagus).

The idea of further increasing tumour dose using LED-SBRT may seem controversial. Currently, SBRT treatment plans are normalized anywhere between the 60% to 90% isodose lines, which can create hotspots on the order of 111% up to a maximum of 167% (Timmerman et al. 2006). While other SBRT protocols do not specifically limit the maximum dose within the PTV (Schuring and Hurkmans 2008). In a recent publication, van Baardwijk et al. (2012) argued against this SBRT prescription philosophy. They completed a systematic review of radiation doses required to eradicate early-stage lung cancer, where they hypothesized that a lower and more uniform dose to the entire PTV may be sufficient to achieve local tumour control and reduce high-grade toxicity. However, conclusions from their study were focused on centrally located tumours only. In clinical practice, alternative fractionation schedules (e.g. 60 Gy in
eight fractions) are generally used for these tumours to reduce surrounding normal tissue toxicity. Clearly, further investigation is required to determine whether additional increases in SBRT tumour dose will lead to further increases in tumour control.

4.2. LED-SBRT and tumour size

In this study, we also varied the size of the tumour from 0.25 cm up to 5 cm within the cylindrical lung phantom. This was done in order to assess the dosimetric effect of tumour size on LED-SBRT derived dose distributions. We classified the tumour size as small (<1 cm), medium (1–3 cm), or large (>3 cm) in accordance with clinical observation of early-staged lung cancers. For small-sized tumours, a minor increase in maximal dose occurred (due to insufficient dose rebuild-up within the tumour) with excellent lung sparing; for medium-sized tumours, increased levels of tumour dose were observed (‘hot-spot’ > 140%) with reduced normal lung dose; and for large tumours, normal lung dose increased (as larger radiation field sizes limits the extent of LED) with minor enhancements in tumour dose. Thus, we hypothesize that LED-SBRT is best suited for treating tumours no larger in diameter than 3 cm, which is applicable to many patients with early-staged lung cancer.

4.3. Dose calculation algorithms for use with LED-SBRT

Dose calculation algorithms can be broadly separated into two classes. The first class of algorithms do not consider electron transport, and can greatly overestimate the lung and tumour dose distribution by as much as 20% for RT conditions involving LED (Engelsman et al 2001). Strictly speaking, class one algorithms should not be used for dose calculation with regard to LED-SBRT.

Unlike class one, class two algorithms model electron transport in an approximate or explicit manner. Clinically accessible algorithms that approximate electron trajectory include: analytical anisotropic algorithm (AAA) (Tillikainen et al 2008), collapsed cone convolution (CCC) algorithm (Ahnesjö, et al 1987), and recently developed Acuros XB (AXB) algorithm (Vassiliev et al 2010). The AAA and CCC algorithm has been deemed acceptable for conditions of moderate electron disequilibrium (Carrasco et al 2004, Hasenbalg et al 2007, Aarup et al 2009, Chow et al 2009), but errors as large as 8% were observed when an 18 MV small field was used to irradiate a lung phantom (Chow et al 2009, Tillikainen et al 2008). In comparison to the AAA and CCC algorithms, the AXB algorithm seems to produce more accurate dose calculations within heterogeneous mediums (Han et al 2011, 2013, Rana and Rogers 2013, Kan et al 2013, Fogliata et al 2011). For example, Han et al 2011, showed better than 2% agreement when comparing dose distributions produced by the AXB algorithm and MC simulation for an 18 MV (2.5 × 2.5 cm²) field incident on a heterogeneous phantom. It appears the AXB algorithm may be appropriate for calculation of LED-SBRT dose distributions in lung. However, a future study would be useful to validate this assertion, and test the accuracy of the AXB algorithm under conditions of extreme LED.

Finally, as the MC technique explicitly tracks electron range (Ahnesjö and Aspradakis 1999), it can accurately predict the dosimetric effects of LED in lung tissue. Recent advances in graphical processing units and parallel computing have made MC VMAT simulations clinically feasible with computation times on the order of seconds (Jia et al 2010, 2011, 2012, Chen et al 2012). Similar MC techniques have already been adopted clinically (e.g. Cyberknife stereotactic radiosurgery system (Accuray Inc., Sunnyvale, CA) (Deng et al 2004)), and will likely be the algorithm of choice for treatment planning of LED-SBRT in the future.
4.4. Clinical implementation of LED-SBRT

Our study used 36 equally weighted square or rectangular fields to simulate an SBRT arc technique. This approach was taken in order to understand the basic physical principals that govern the dose distribution within the lung and tumour tissues. In reality, modern day SBRT techniques employ volume modulated arc therapy (VMAT) (Otto 2008, Chin and Otto 2011) and/or intensity-modulated radiation therapy (IMRT) (Videtic et al 2010), which are capable of optimizing the dose distribution with respect to specific constraints. A future study involving a MC modelled, LED-optimized, VMAT technique (Lobo and Popescu 2010) may be useful to further improve the tumour-to-lung dose ratio.

Beyond dose optimization techniques, the LED phenomenon could be further exploited by gating the SBRT delivery. As the extent of LED is inversely related to lung density, further reductions in lung dose could be gained by delivering the radiation during an *inhale* phase of the breathing cycle (i.e. respiratory gating the radiation treatment). For instance, Hanley *et al* 1999 and Yorke *et al* 2002 have proposed using a deep inspiration breath-hold (DIBH) technique for radiation therapy of lung cancer. Hanley *et al* suggest that lung density can be reduced from 0.26 to 0.19 g cm$^{-3}$ using DIBH. Also it was reported that DIBH immobilizes the target, improving tumour localization, and allows for target margin reduction. With LED-SBRT, internal target volume reduction should be pursued (via 4DCT and gating) in order to reduce the tissue heterogeneity of the PTV, and localize high dose levels within the tumour volume.

Unfortunately, gated LED-SBRT will involve longer treatment times, which will be compounded by attempts to increase tumour dose levels. A large dose rate is required in order to deliver a sufficient amount of monitors units through a small field aperture. This may be conceivable using the TrueBeam LINAC in flattening filter free mode where dose rates can be up to four times larger (at certain energies; 6 or 10 MV) than traditional LINAC technology (Hrbacek *et al* 2011). Before LED-SBRT can be implemented clinically, a future study is required to resolve issues involving: (1) limitations concerning tumour size and location within the thorax, (2) toxicity levels in adjacent healthy tissues, (3) gating and choice of breathing phase, (4) MC VMAT optimization, and (5) clinical time constraints given the necessity of high dose rates.

5. Conclusion

This article introduces a novel SBRT technique for application to patients with early-staged lung cancer. By exploiting the LED phenomenon, we have demonstrated the possibility of increasing tumour dose while maintaining or lowering normal lung dose levels. Future work is required to determine the limitations of LED-SBRT implementation within a clinical environment, and resolve the controversy concerning toxicity of adjacent healthy tissues.

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