STANDARD PROTOCOL

<table>
<thead>
<tr>
<th>Document Title:</th>
<th>Pre-operative concurrent chemoradiotherapy for superior sulcus non-small cell lung cancers</th>
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<tbody>
<tr>
<td>Document Type:</td>
<td>Clinical Guideline</td>
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<tr>
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<td>Author(s):</td>
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</table>

**Standard care plan for induction concurrent chemoradiotherapy for superior sulcus non-small cell lung cancer**

**References**


Patient selection

- Superior sulcus tumours potentially suitable for surgical excision ie fit for radical surgical approach following concurrent chemoradiotherapy
- Histologically confirmed NSCLC
- T3-4 pN0 M0 (pN0 status to be confirmed by a mediastinoscopy/EBUS)
- Patients considered technically and medically operable
- WHO performance status 0-1 (appendix 1) and no significant co-morbidities that might impact on tolerability and toxicity of treatment
- Lesion not within a previous radical radiotherapy field
- Radiotherapy target volume is likely to meet radiotherapy planning constraints as judged by a clinical oncologist

Cautions

- Adequate renal function for platinum chemotherapy - defined by GFR > 50 ml/min. The Cockcroft and Gault formula should be used to estimate GFR, but if < 60 ml/min then an EDTA should be performed
- Patients with the following characteristics are not eligible: medically unstable (e.g. unstable diabetes, uncontrolled arterial hypertension, infection, untreated hypercalcaemia or ischaemic heart disease) or any other condition that would limit the ability to tolerate concurrent chemoradiotherapy.
- Adequate lung function (typically FEV1 >40% predicted and KCO >40% predicted). However, the evidence for correlation of lung function with respiratory toxicity is poor. Hence, these parameters serve only as a guide.

Evidence

A lack of clinical trials makes comparisons between different treatment modalities very difficult. Management to date has largely been based on retrospective experience of large single institutions. The bimodality approach of induction radiotherapy followed by surgical resection has been the accepted standard of care for the last 50 years. However, the trimodality approach of induction concurrent chemoradiotherapy followed by surgical resection has now reported improved outcomes in carefully selected patients. The number of patients suitable for trimodality treatment is very small, but for these patients it should be considered the standard of care.
Outcome

In selected patients, radical radiotherapy alone can achieve 5YS of 15-25% and induction radiotherapy followed by surgical resection can achieve 5YS of 30%. Recently, two prospective series using trimodality approach of induction concurrent chemoradiotherapy followed by surgical resection (followed by two further cycles of adjuvant chemotherapy) has reported 5YS of 44-56%.

Toxicity

The trimodality approach has mortality of 2.7-6.9% with major complication rate of 10.3-45%. The induction chemoradiotherapy component has significant associated mortality (1.2-2.7%). Myelosuppression is common and G3-4 oesophagitis is reported in 0-16%. The latest estimates of spinal cord tolerances for radiotherapy alone were recently published by Schultheiss. The probability of myelopathy at 50Gy is 0.2%. The dose for 5% myelopathy is 59.3Gy and the D50 is 69.4Gy. However, it is imperative to be cautious using concurrent chemoradiotherapy.

1. Initial investigations and work up prior to start of treatment

**Diagnostic investigations and work up should usually include:**

- A chest x-ray,
- Full blood count and full biochemical profile including liver and bone markers
- Stage of disease determined and documented
  - CT Abdomen/thorax
  - Bronchoscopy (if tumour likely to be accessible)
  - PET-CT
  - Magnetic resonance Imaging (MRI) should be performed to assess chest wall and brachial plexus involvement prior to surgery
  - Sampling of radiologically suspicious mediastinal lymph nodes with mediastinoscopy or endobronchial ultrasound (EBUS).
  - Biopsy of supraclavicular lymph node if radiologically suspicious of malignancy
  - Brain scan (CT or MRI) as with all concurrent schedules
- Pathology/Cytology confirmed diagnosis of NSCLC
- FEV1 and DLCO (transfer factor) desirable
- Other scans (bone scan) should only be requested if clinically indicated
- Clinical assessment and documentation of current disease related symptoms
- Performance status recorded
- Co-morbidities recorded
- Smoking status recorded
- FH recorded
- Concomitant medications recorded and stopped if necessary
- Patient consented for aims, practicalities and toxicity of concurrent chemoradiotherapy
- Plan confirmed with consultant oncologist if 1st seen by junior college
- All patients undergoing concurrent chemo-radiotherapy should have a Treatment Plan completed at the outset (appendix 2)
Non-small cell lung cancers of the superior sulcus should be discussed in detail at a fully accredited Lung MDT and patients should be assessed for surgical suitability by a Thoracic Surgeon. Gold standard treatment is pre-operative concurrent CTRT followed by resection where possible +/- adjuvant chemotherapy.

2. Treatment

2.1. Treatment summary for PE concurrent with RT for NSCLC of the superior sulcus (appendix 3)

All concurrent chemo-radiotherapy should be delivered at The Christie. Patients will be managed jointly by the clinical oncology and medical oncology teams.

2.2. Chemotherapy

Two cycles of chemotherapy are given concurrently with weeks 1 and 5 of radiotherapy. The concurrent chemotherapy regimen used is:

- Etoposide 50 mg/m² iv: day 1-5 and 29-33
- Cisplatin 50 mg/m² iv: day 1, 8, 29, 36

Prophylactic antibiotics such as ciprofloxacin or levofloxacin are recommended. For full chemotherapy regimen details (appendix 4)

Chemotherapy dose modifications

When dose modifications are required, the aim should be to delay and give at full dose rather than reducing the dose. The need for dose modification should be based on clinical judgment and the recommendations in appendix 5.

Consolidation Chemotherapy

Patients will be reassessed after surgery by the treating oncologist. Based on the level of fitness after surgery, patients may be offered two additional cycles of Cisplatin/Etoposide

- Etoposide 50 mg/m² iv: day 1-5 and 29-33
- Cisplatin 50 mg/m² iv: day 1, 8, 29, 36 with hydration

2.3. Thoracic Radiotherapy

For full radiotherapy technique including verification is described in appendix 6. Radical radiotherapy should start on day 1 of the first cycle of chemotherapy. Every effort should be made to start concurrent chemoradiotherapy on a Monday. The total dose of radiotherapy will be 45 Gy in 25 daily fractions of 1.8 Gy, prescribed at the ICRU reference point.

On-Treatment Assessments

During concurrent chemo-radiotherapy patients should be assessed at least on a weekly basis as per agreement between the medical and clinical oncologist and should include:

- Clinical assessment including performance status and weight
- FBC/Biochemical profile
- CXR if worsening dyspnoea
2.4. Surgery

**Surgical Assessment**
Patients are to be reviewed surgically as soon as the chemoradiotherapy is completed. If surgery felt not to be possible for technical or medical reasons, the radiotherapy is to be continued to the dose of 60-66 Gy in 2Gy fractions.

2.5. Follow up

Patients should be seen by ideally by the treating clinical oncologist 6 weeks following completion of chemoradiotherapy. Thereafter, follow-up is as per local agreement between the respiratory physicians, oncologists and surgeons (if surgery undertaken). A typical schedule may be 3 monthly in the 1st year, 4 monthly within the 2nd year, 6 monthly in the 3rd year and annually in the 4th and 5th year of FU.

Serial CXRs are recommended. A CT scan, at 3 months post-completion of treatment, may be helpful as a baseline in patients for whom further treatment would be appropriate should they relapse. CT scans may be done at any point if there is suspicion of relapse clinically on CXR.

**APPENDICES**

**APPENDIX 1**

<table>
<thead>
<tr>
<th>Grade</th>
<th>ECOG PERFORMANCE STATUS*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Fully active, able to carry on all pre-disease performance without restriction</td>
</tr>
<tr>
<td>1</td>
<td>Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work</td>
</tr>
<tr>
<td>2</td>
<td>Ambulatory and capable of all self care but unable to carry out any work activities. Up and about more than 50% of waking hours</td>
</tr>
<tr>
<td>3</td>
<td>Capable of only limited self care, confined to bed or chair more than 50% of waking hours</td>
</tr>
<tr>
<td>4</td>
<td>Completely disabled. Cannot carry on any self care. Totally confined to bed or chair</td>
</tr>
<tr>
<td>5</td>
<td>Dead</td>
</tr>
</tbody>
</table>
APPENDIX 2. Treatment Plan for concurrent chemo-radiotherapy in NSCLC.

Treatment Plan NSCLC
Concurrent Chemo-Radiotherapy

Chemotherapy – Cisplatin & Etoposide

- Radiotherapy planning scan date……………………………………
- Provisional thoracic radiotherapy start date…………………………

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Chemotherapy dates</th>
<th>Radiotherapy dates</th>
<th>Comments (eg RT start date)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Planned</td>
<td>Actual</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Date thoracic radiotherapy delivered: ........to ........ #............

Notes:
- When start date is given for radiotherapy please inform Medical oncologists so that they can arrange chemotherapy.
- Chemotherapy regime will be Cisplatin & Etoposide day 1, Etoposide days 2 to 5, and Cisplatin day 8.
- Both chemotherapy and radiotherapy will start on the same day.
- Chemotherapy is given for 2 cycles only. Cycles are 4 weekly.
APPENDIX 3: Treatment summary for concurrent chemoradiotherapy for superior sulcus tumours

<table>
<thead>
<tr>
<th>Week</th>
<th>Activity</th>
</tr>
</thead>
</table>
| 1 – 5 | Start Monday: **Radiotherapy daily 1.8 Gy in 25 fractions**  
**D1-5, 28-33 etoposide & D1, 8, 29, 36 cisplatin chemotherapy:**  
- with antiemetics;  
- consider antibiotic prophylaxis and a PPI.  
Weekly review by doctor including FBC, biochemistry and weight  
CXR Week 4 before chemotherapy cycle 2 |
| 7 | Restaging CT scan thorax / abdomen |
| 8-10 | Surgery  
**If not operable,** continue radical radiotherapy to dose of 60-66Gy in 30-33 daily fractions (excluding weekends) |
| 12-16 | Consolidation chemotherapy (at the discretion of the clinicians)  
2 cycles of cisplatin and etoposide  
Week 12 and week 16-cisplatin d1 and d8; etoposide days 1-5 |
| Follow up | Weekly until acute toxicities resolve  
3 monthly for 1 year, 6 monthly years 2 and 3, then annually to 5 years.  
CT scan thorax and abdomen at 12 months |

**Pretreatment**
1. Baseline assessment, consultation and consent by clinical and medical oncologist  
2. RTP scan  
3. When start date is known book in patient chemotherapy ward bed (for first night if patient prefers, thereafter can administer outpatient CT)  
Book CT scan for week 6 if desired (not mandatory). Consider MRI
APPENDIX 4: Cisplatin and Etoposide concurrent regimen – as per concurrent regimen for all non-small cell lungs cancers

Dosages:
- Cisplatin 50mg/m² on days 1 and 8, Etoposide 50mg/m² on days 1-5
- Radiotherapy 45 Gy in 25 fractions commencing with chemotherapy for superior sulcus tumours
( NB standard concurrent without surgery has dose of 60-66Gy in 30-33 fractions)

Regimen:

<table>
<thead>
<tr>
<th>Order</th>
<th>Fluid/Drugs</th>
<th>Dose</th>
<th>Volume</th>
<th>Route &amp; Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>Sodium Chloride</td>
<td>0.9%</td>
<td>1000ml</td>
<td>IVI</td>
</tr>
<tr>
<td>1</td>
<td>Potassium Chloride</td>
<td>20mmol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Sodium Chloride</td>
<td>0.9%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Magnesium Chloride</td>
<td>1g</td>
<td>1000ml</td>
<td>IVI</td>
</tr>
<tr>
<td></td>
<td>90 minutes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cisplatin</td>
<td>50mg/m²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Sodium Chloride</td>
<td>0.9%</td>
<td>1000ml</td>
<td>IVI</td>
</tr>
<tr>
<td></td>
<td>Etoposide</td>
<td>50mg/m²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 2-5</td>
<td>Sodium chloride</td>
<td>0.9%</td>
<td>500ml</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td>Etoposide</td>
<td>50mg/m²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 8</td>
<td>Sodium Chloride</td>
<td>0.9%</td>
<td>1000ml</td>
<td>IVI</td>
</tr>
<tr>
<td>1</td>
<td>Potassium Chloride</td>
<td>20mmol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Sodium Chloride</td>
<td>0.9%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Magnesium Chloride</td>
<td>1g</td>
<td>1000ml</td>
<td>IVI</td>
</tr>
<tr>
<td></td>
<td>90 minutes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cisplatin</td>
<td>50mg/m²</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mannitol</td>
<td>20%</td>
<td>200 ml</td>
<td>IVI</td>
</tr>
<tr>
<td>3</td>
<td>Sodium Chloride</td>
<td>0.9%</td>
<td>1000ml</td>
<td>IVI</td>
</tr>
<tr>
<td></td>
<td>Potassium Chloride</td>
<td>20mmol</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Number of Cycles and Scheduling:
- 2, q28 days

Associated medication:
- Ondansetron 8mg IV bolus Dexamethasone 8mg IV bolus pre-chemotherapy days 1 and 8
- Dexamethasone 8mg po bd for 3 days starting 24 hours before chemotherapy
- Consider prophylactic antibiotics if obstructing tumour/presence of consolidation/collapse/cavitation: levofloxacin 500mg od starting on day 8 for 10 days

Expected toxicity:
Emesis (severe), alopecia (total), myelotoxicity (moderate-severe), nephrotoxicity, pneumonitis, oesophagitis, ototoxicity, peripheral neuropathy, infertility

**Required investigations pre-treatment:**
- Full lung function including transfer factor
- Histology
- CT or PET-CT staging including brain scan
- eGFR/EDTA clearance

**On-treatment assessments:**
- Clinical assessment on a weekly basis during therapy – Monday am clinic
- CXR with each cycle
- Complete CTRT toxicity sheet with each assessment
APPENDIX 5. Recommendations for chemotherapy dose modifications during concurrent chemo-radiotherapy for NSCLC and SCLC.

Haematological Toxicity:

<table>
<thead>
<tr>
<th>ANC x 10^9/l</th>
<th>Platelets x 10^9/l</th>
<th>Cisplatin /Etoposide</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 1.5</td>
<td>and</td>
<td>≥ 100</td>
</tr>
<tr>
<td>≤ 1.5</td>
<td>or</td>
<td>≤ 100</td>
</tr>
</tbody>
</table>

Febrile neutropenia or grade 4 neutropenia > 7 days or Grade 4 platelets or ≥ grade 2 bleeding with thrombocytopenia Recommend once ANC >1.5 and Platelets > 100 at full dose with GCSF support or at 75% dose

Hepatic Toxicity:

<table>
<thead>
<tr>
<th>Raised AST/ALT</th>
<th>Raised Bilirubin</th>
<th>Cisplatin</th>
<th>Etoposide</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 3.0 x ULN</td>
<td>and</td>
<td>&lt; 1.5 x ULN</td>
<td>Full dose</td>
</tr>
<tr>
<td>≥ 3.0 x ULN</td>
<td>or</td>
<td>≥ 1.5 x ULN</td>
<td>Delay one week then reassess using the same criteria; if delayed for two weeks discontinue</td>
</tr>
</tbody>
</table>

Renal Toxicity:

If estimated CrCl < 60ml/min, an EDTA should be requested prior to each cycle

<table>
<thead>
<tr>
<th>CrCl/GFR (ml/min)</th>
<th>Cisplatin</th>
<th>Etoposide</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 60</td>
<td>100%</td>
<td>Full dose</td>
</tr>
<tr>
<td>50-59</td>
<td>100%</td>
<td>Full dose</td>
</tr>
<tr>
<td>45-49</td>
<td>50% or substitute with carboplatin AUC 5</td>
<td>75% dose</td>
</tr>
<tr>
<td>&lt; 45</td>
<td>Discontinue</td>
<td>discontinue</td>
</tr>
</tbody>
</table>

Other Toxicity

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 2 peripheral neuropathy</td>
<td>Substitute carboplatin AUC 5 or 50% cisplatin dose after recovery to ≤ grade 1; 100% dose of etoposide</td>
</tr>
<tr>
<td>Any grade 3-4 toxicities except mucocitis and oesophagitis</td>
<td>75% previous dose of cisplatin, etoposide after recovery to ≤ grade 1</td>
</tr>
<tr>
<td>Any diarrhoea requiring hospitalisation or Grade 3-4 diarrhoea</td>
<td>75% previous dose of cisplatin/etoposide after recovery to ≤ grade 1</td>
</tr>
<tr>
<td>Grade 3-4 musocitis</td>
<td>75% previous dose of etoposide and 100% previous dose of</td>
</tr>
</tbody>
</table>
Oesophagitis

In the event of grade 3 oesophagitis, chemoradiotherapy should be suspended until resolution to ≤ grade 1. The decision to recommence treatment should be at the discretion of the clinician. In the event of grade 4 oesophagitis, chemoradiotherapy should be discontinued.

Pneumonitis

In the case of grade ≥ 3 toxicity, treatment should be discontinued.
APPENDIX 6

Radical Radiotherapy Technique for NSCLC


Treatment will be 3-D conformal radiotherapy (or intensity modulated radiotherapy (IMRT) if dose constraints cannot be met with conventional treatment planning).

**Patient treatment position and set-up**

http://discover/departments/radiotherapy/docs/work_instructions/LEVEL3/191.3.doc

Supine, breathing normally using an external immobilisation device with arms by side and using a 5-point thermoplastic shell to aid stability in most cases. Very occasionally arms may be up using an inclined lung board as per standard for non-apical tumours. Set up should be by reference to anterior and lateral tattoos on stable areas of skin and bony anatomical landmarks and reference points on the shell.

**Patient data acquisition**

A planning CT scan should be performed in the treatment position, whilst the patient undertakes normal respiration (http://discover/departments/radiotherapy/docs/work_instructions/LEVEL3/191.3.doc) The whole lung (cricoid to L2) should be imaged using 0.3 cm slices to allow dose-volume histograms to be calculated. IV contrast is used if the patient has central disease invading the mediastinum and to aid delineation of organs-at-risk such as brachial plexus using subclavian vessels as surrogate marker for this. 4D CT scan may be used if available (http://discover/documents/default.aspx?Details=Y&Doc_ID=5979).

**Target volume delineation**

Treatment will be planned based on information from radiological imaging (including PET-CT and MRI thoracic inlet) and if performed additionally, bronchoscopy. Target volume delineation will be done using both the mediastinal and lung windows.

Gross Tumour Volume (GTV) is defined as the identifiable tumour (NB: patients should be N0 and therefore for this scenario there should be no nodes within the GTV). Elective nodal irradiation should not be employed.

Clinical target volume (CTV) comprises the GTV with a 0.5 cm margin of radiologically normal tissue in all directions. It will take into account microscopic spread. Manual adjustment of CTV is permitted to reduce dose to the spinal cord for example, when disease is adjacent to a structure such as a vertebra but is not thought to invade the structure.

The planning target volume (PTV) comprises the CTV with a 1.3 cm margin superiorly and inferiorly, and 1 cm margin transaxially. Reduction of the CTV to PTV expansion is not permitted.

Internal target volume (ITV) is only created if using a 4D CT scan. It is defined as the identifiable tumour based on delineation using 4D CT scan maximum intensity projection images. The expansion margins differ from above as respiration is already taken into account.
Hence expansion of ITV to CTV is + 0.5cm in all directions, CTV to PTV expansion is + 9mm superiorly and inferiorly and + 7mm transaxially.

**Organs at risk (OAR) - delineation and dose constraints**

Critical normal structures are the spinal cord, lung, heart, brachial plexus and oesophagus. Dose volume histograms (DVH) for the normal lung tissue and spinal cord and will be calculated. The oesophagus and heart should also be contoured if using intensity-modulated radiotherapy. Additionally, for superior sulcus tumours, the brachial plexus should be outlined as an OAR.

**Lungs:** contour all inflated right and left lung as one structure using lung windows. The V20 should be <35% in conventional fractionation (i.e. <35% of the volume of “normal” lung, excluding PTV, should receive a dose of ≥20Gy). The mean lung dose should be <20Gy.

**Spinal cord:** contour based on the bony limits of the spinal canal. Delineation of the spinal cord should extend at least 10cm beyond the superior and inferior extent of the PTV. Maximum radiation dose to spinal canal should not exceed 48Gy in conventional fractionation. For patients on conventionally fractionated concurrent chemoradiotherapy, as in this scenario, a planning-at-risk volume (PRV) is created. This PRV is the canal + 0.5cm transaxially and the dose should not exceed 54Gy.

**Oesophagus:** contoured using mediastinal windows from cricoid cartilage to the gastro-oesophageal junction. Planning should aim (not mandatory) to limit the length of treated oesophagus to 120 mm within the PTV and aim to limit the volume treated with doses ≥50Gy. Due to lack of clear evidence regarding toxicity correlation with oesophageal dose volume histogram data, if these parameters are exceeded the clinician may proceed with radiotherapy at their discretion.

**Heart:** contour along with the pericardial sac. The superior aspect (ie base of heart) for contouring purposes will begin at the level of the superior aspect of the left atrium and extend inferiorly to the apex of the heart. The heart can receive the total dose (TD) to < 30% of its volume. For > 50% of cardiac volume, dose < 50% of TD is recommended.

**Brachial plexus:** only the major trunks of the brachial plexus should be contoured using the subclavian and axillary vessels as a surrogate for identifying the location of the brachial plexus. This neurovascular complex will be contoured following along the route of the subclavian vein/artery to the axillary vein ending after the neurovascular structures cross the 2nd rib.

The standard accepted tolerance of the brachial plexus has been between 55-60Gy in conventional fractionation without chemotherapy (TD5/5). Recent studies suggest that it may actually be higher than this. Given that the main aim is tumour control in a region of close proximity to the brachial plexus, these limits may be exceeded. It is good practice to limit the dose where possible to the brachial plexus. However, tumour control versus risk of plexopathy is a difficult issue and careful patient consent is imperative.

If dose constraints cannot be met using 3D-conformal radiotherapy, intensity-modulated radiotherapy (IMRT) should be considered to optimize the dose distribution.

**Dose prescription**

The dose will be specified at the ICRU reference point according to ICRU 50, 62 and 83 and fully corrected for inhomogeneity. A DVH for the PTV should be calculated. The dose distribution within the PTV should ideally be within ±5% of the prescribed dose, and no
more than ± 7% of the prescribed dose. Wedges, tissue compensators or multi-leaf collimators may be used to achieve homogeneity of dose.

**Neo-adjuvant concurrent chemoradiotherapy doses:** 45Gy in 25 daily fractions over 5 weeks.
If surgery is subsequently not feasible the radiotherapy should be completed using conventional fractionation to a total dose of 60-66Gy in 30-33 daily fractions. The aim would be to re-start radiotherapy as soon as possible if surgery is not deemed possible.

**Verification:**

Standard departmental policy dictates consecutive portal imaging on days 1-3 of radiotherapy to confirm set-up accuracy and once weekly thereafter. If a discrepancy of ≥ 5 mm is found then set-up should be corrected and re-imaged as above.
Alternatively, patients may be verified using cone-beam imaging with the same frequency and tolerance.


**Treatment Delays:**

Every effort should be made to deliver the prescribed dose of radiotherapy within the standard timeframe. If unavoidable delays occur, that could increase the overall treatment time beyond the specified period, e.g. due to machine breakdown, compensation should if possible be made by one of the following mechanisms:
- giving two fractions on a subsequent day, with a minimum interval of six hours between fractions, **or**
- treating on a weekend day, **or**
- if conventional fractionation – adjustment of fraction size (ensuring remains <2.5Gy) to deliver the total prescribed dose within 33 days.

**On treatment assessments**

**Weekly clinical assessment by medical team including**
- Graded documentation of toxicity
- Assessment of disease related symptoms
- Performance status recorded

**Management of treatment related toxicity**

| CTCAE v4.0 Skin and Subcutaneous Tissue Disorders |
|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Adverse Event            | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
| Oesophagitis             | Asymptomatic; clinical or diagnostic observations only; intervention not indicated | Symptomatic; altered eating/swallowing; oral supplements indicated | Severely altered eating/swallowing; tube feeding; TPN or hospitalization indicated | Life-threatening consequences; urgent operative intervention indicated | Death |

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27/03/2015
## Radiation oesophagitis
- Grade 2 oesophagitis – optimise analgesia (consider sucralfate suspension, paracetamol mucilage, codeine phosphate liquid, oromorph, fentanyl patch). Advise soft diet/oral dietary supplements if required. Empirical fluconazole may be advised.
- Grade 3 oesophagitis - treat as for grade 2 oesophagitis but also consider admission to The Christie/dietician input/parenteral nutrition if required. Every effort should be made to continue radiotherapy. Avoid placement of naso-gastric tubes
- Grade 4 oesophagitis – As for grade 3 oesophagitis but radiotherapy should be stopped.

## Radiation Pneumonitis
- Grade 2 pneumonitis - Consider oral steroids/antibiotics/antifungals
- Grade 3 pneumonitis – consider admission to The Christie for high dose IV steroids/oxygen/antibiotics/antifungals. Alert critical care team. Consider stopping radiotherapy
- Grade 4 pneumonitis – as for grade 3 but will require admission to critical care and consider ventilatory support if appropriate. Stop radiotherapy.

## Radiation dermatitis
- Topical treatment with aqueous cream/1% hydrocortisone cream if required