Radiotherapy for lung cancer

Lung cancer is a common cancer in the Western world and continues to be a huge burden on the National Health Service in the UK. There are two broad histological categories of lung cancer, namely small cell and non-small cell. Non-small cell lung cancer (NSCLC) makes up the majority of lung cancer incidence and contains a number of different subtypes such as adenocarcinoma, squamous cell carcinoma and large cell carcinoma.

Small cell lung cancer is a more chemosensitive disease but consolidation radiotherapy is given to a subset of these patients to reduce risk of relapse, as well as prophylactic cranial irradiation (PCI). PCI will reduce the incidence of intra-cranial metastases in small cell lung cancer patients and has also shown a survival advantage.1

Staging for NSCLC is based on TNM Classification as stipulated by the International Staging System for Lung Cancer. TNM Classification stratifies disease in terms of Tumour, regional Nodes and distant Metastasis.2 T stage can be graded from 0 to 4 and is determined by size of the tumour and its invasion into surrounding structures. N stage is graded from 0 to 3 depending on the involvement of nodal groups in close proximity or further away from the primary tumour. M staging is either M0 (no distant metastases) or M1 (presence of distant metastases). The TNM groupings are then further subdivided into Stage I, II, III, and IV. Stage I, II, and IIIA are suitable for treatment with radical radiotherapy. Patients with locally advanced NSCLC (ie involvement of tumour without invasion into major surrounding structures +/- local lymph node involvement) are candidates for either surgery or radical radiotherapy. If surgery is technically not possible or the patient is not medically fit to undergo surgery, radical radiotherapy is the treatment of choice.

Role of radical radiotherapy in treatment of lung cancer

The majority of patients who receive radical radiotherapy as their definitive treatment for NSCLC are those with locally advanced disease. These are patients whose disease is limited to the thorax but is too extensive for surgical resection and usually have bulky Stage II-III lesions. These patients will receive combination treatment with platinum-based chemotherapy and radical radiotherapy, treating to a total dose in the region of 64 Gray in 32 fractions (figure 1). In the UK, radiation is usually delivered on a once daily basis for a total of six and a half weeks (excluding weekends). The daily treatment time is approximately seven to 10 minutes.

A proportion of patients with Stage I and II disease will be unsuitable for surgery due to poor lung function or other medical problems and these patients are often suitable for treatment with radical radiotherapy. The optimum form of radiation treatment for these patients is stereoeblative radiotherapy (SABR). This is a relatively new radiation technique for lung cancer patients and is a precise way of treating peripheral tumours without loco-regional lymph node involvement with doses of radiation above that which we normally use with conventional radiotherapy techniques (figures 2 and 3). The treatment is delivered over three to five fractions of treatment with typical doses of 12-20Gy per session. With conventional radiotherapy we treat with daily treatments of 2Gy. The results for SABR have been very...
A patient being treated with SABR on a conventional linear accelerator with IGRT capabilities immobilised on a custom-made thoracic board.

Successful and superior to conventional radiotherapy, with local control rates in the region of 85% and therefore more comparable with surgery. International multi-centre trials are under way comparing SABR with curative surgery in early lung cancer patients. SABR requires specialist positioning equipment and imaging to confirm correct targetting. The treatment can be delivered on a conventional linear accelerator or newer generation machines such as Cyberknife. Some patients are not suitable for SABR and can be treated with conventional radiotherapy alone. If the volume to be irradiated is small, the radiation may be hypofractionated to reduce the overall treatment time, treating with 55 Gray in 20 fractions over four weeks. If the volume is large, a similar regime to that used for locally advanced Stage III disease can be implemented.

Radiotherapy is also useful in the palliative setting. It can be very effective at controlling distressing symptoms in patients with advanced stage lung cancer such as pain, haemoptysis, superior vena cava obstruction and bone and brain metastases.

**Target volume definition**

Target volume definition is an essential part of the radiotherapy planning process and obviously impacts on response and progression rates. It is important to correctly and accurately define the target volume, allowing for tumour motion with respiration, and cover all involved disease as well as considering treatment of at risk tissue and nodes. CT scanning is the primary imaging modality used to define target volumes for radiation. The target volumes GTV, CTV and PTV can be delineated on CT.

Current methods for target volume definition

Three target volume definitions are stipulated by the International Commission on Radiation Units (ICRU) reports 50 and 62 to aid in radiotherapy planning. These are: gross tumour volume (GTV) which includes the macroscopic tumour as visible on examination of the patient and using imaging scans; the clinical target volume (CTV) which is the GTV with a margin added to account for microscopic spread of malignant cells around the tumour; and planning target volume (PTV) which constitutes the CTV with a margin added for internal organ motion and technical radiation set-up errors. The ICRU 62 report includes an additional volume between CTV and PTV, called the internal target volume (ITV) that takes into account respiratory and cardiac induced movement.

**New techniques in radiotherapy planning**

Techniques for delivering radiation have improved dramatically over the last 10-15 years. The advent of 3D conformal radiotherapy with CT planning has revolutionised radical radiotherapy and has enabled us to give high doses of radiation with acceptable normal tissue toxicity. The technique uses target volumes delineated on CT slices at multiple levels through the patient over the region of interest, on which normal structures are also outlined. A plan can then be constructed using multiple fields to treat the lung tumour according to the delineated CTV while calculating the dose of radiation to the organs at risk. Following on from 3D conformal radiotherapy, many centres now use 4DCT acquisition and planning techniques. In 4DCT acquisition the patient is scanned over a number of breathing cycles and the respiratory motion of the tumour and lungs measured by an external surrogate placed on the patient’s surface and/or an internal fiducial marker. The respiratory cycle is divided into eight to 12 phases and CT data captured over a number of breathing cycles. The data is then retrospectively binned into the correct position in the respiratory cycle to create a movie loop of the tumour and lungs over the breathing cycle. This allows an accurate patient-specific assessment of tumour motion which is used in creating an ITV for planning the radiotherapy treatment.

The relatively new technique of intensity modulated radiotherapy (IMRT) – intensity modulation within a radiation beam – is designed on the basis of the target prescription and a set of dose constraints for sensitive structures using inverse planning algorithms. The capability of differentiating the weight of individual rays of a beam in IMRT allows sculpting of the isodose distributions to achieve maximum dose conformity. IMRT has been used with considerable success in certain tumour sites including head & neck and prostate cancer. IMRT can also be useful in the treatment of certain lung cancer patients. The issues to consider are the motion of the tissues and inhomogeneity of the region, which may cause dose deviation and uncertainty, causing adverse effects on both tumours and normal tissue.

**Lung motion measurement during treatment delivery**

There are a number of ways of manipulating the respiratory cycle and the treatment machines in order to minimise movements of the tumour during radiotherapy treatment.

The basic concepts are to:

a, treat the patient only at certain points in the respiratory cycle governed by tumour tracking systems or controlling the patient’s breathing, eg respiratory gating technique or

b, artificially stop the patient breathing (ABC technique).

Active breathing control (ABC)

Lung tumours move significantly with respiration and it is therefore necessary to add a margin around the CTV to allow for this phenomenon. As large areas of normal lung are irradiated, the dose of radiation that is given in radical treatment is compromised due to the tolerance of normal tissue.

The ABC apparatus aims to minimise the margin for breathing motion by stopping the breathing at specific points in the respiratory cycle. The ABC apparatus consists of a modified ventilator with two separate flow monitors and two ‘scissor valves’ to monitor and control inspiration and expiration independently. The flow signals are digitised to enable lung volumes to be calculated. The user can then open or close the valves to specify the duration of active breathhold. The patient can also see a real time display of the changing lung volumes.

Respiratory gating techniques

Various methods have been employed recently to attempt to reduce the CTV to PTV margin in lung cancer. One technique is the utilisation of gated radiotherapy. The basic concept of this technique is to gate the radiation beam in some way as the patient breathes freely. The method requires real time monitoring of the patient’s breathing, which can be achieved in a number of ways.

One example is the Varian Medical Systems respiratory gating equipment. The gating system includes an infrared camera mounted inside the treatment room connected to a laptop. The patient has a plastic box with a pair of reflective
markers on their abdominal surface. The motion of the marker is tracked using software supplied by the system. As the patient breathes, a sinusoidal graphical representation of the patient's breathing is visible which can be correlated to the diaphragm position viewed fluoroscopically or on CT. The radiographer monitors the patient's breathing and manually initiates the beam-on condition once the breathing pattern is constant and periodic. The linear accelerator will trigger the beam-on condition within the specified gated interval.

Set-up error and image guided radiotherapy (IGRT)

Internal movements must be considered on a daily basis during radiation treatment. The patient's position for treatment must be comfortable, reproducible and suitable for acquisitions of images for planning and treatment delivery. External movement is minimised using devices such as a customised thoracic boards and/or vacuum-assisted immobilisation devices.

The PTV includes set-up error and organ movement:

1. Set-up error includes transfer of information from simulation to CT scanner, reproducibility of patient position from day-to-day which is affected by immobilisation techniques. Permanent skin marks (radiation tattoos) are used to set-up patients. These marks are 2-3mm in diameter and the skin itself is not a rigid structure and will be affected by obesity, posture, muscle tone etc. The room lasers which are used in most departments when setting up patients for treatment have a degree of inaccuracy associated with them which will also add to set-up errors.

2. Organ motion is dependent on a variety of factors. These include location of the tumour in the lung, fixation to adjacent structures, lung capacity and pre-existing lung disease, patient fixation and patient anxiety. In the last 5-10 years most radiotherapy departments have invested in IGRT equipment. This consists of a linear accelerator with on-line imaging capacity. An example is the Elekta Synergy kilovoltage cone-beam CT and linear accelerator. Regular images can be taken on a patient receiving radical radiotherapy for lung cancer and directly compared to the radiotherapy planning CT to ensure concordance of the anatomy. Software programmes will inform treating radiographers of the shifts that may be required to achieve concordance before the patient is treated.

Conclusion

Radiotherapy has an important role in the treatment of lung cancer in both the curative setting and for palliation of symptoms. There are many areas of research in imaging and radiotherapy treatment of lung cancer that are current and evolving. This information can then be used to improve radiotherapy planning and treatment in patients receiving radical radiotherapy for lung cancer.

References