Isotoxic Radiotherapy Planning for Non-Small Cell Lung Cancer: Is IMRT The Answer?

Lay summary
This project will investigate two different methods for giving external beam radiotherapy to patients with non-small cell lung cancer (NSCLC). In particular, it will be looking at how to give isotoxic radiotherapy. In isotoxic radiotherapy, the dose of radiotherapy given to the tumour is different for each patient, and is determined by assessing how much dose the patient’s healthy tissues can tolerate without bringing about any lasting side effects. This research will investigate which type of radiotherapy treatment delivery (3-dimensional conformal radiotherapy (3DCRT) or Intensity Modulated Radiotherapy (IMRT)) will allow more patients to receive the highest dose that can be delivered (76Gy in 20 fractions or equivalent). The study will also look at why IMRT needs to be used instead of 3DCRT for certain patients.
Principal Aim of the Study
To investigate the targeted use of Intensity Modulated Radiotherapy (IMRT) to treat Non Small Cell Lung Cancer (NSCLC) patients with isotoxic lung radiotherapy. To quantify the effect that IMRT will have on the ability to escalate prescribed dose whilst keeping dose to normal tissues below tolerance levels.

Primary Research Question: Are patients more likely to achieve a dose escalation to 76 Gy in 2 Gy per fraction (or biological equivalent) if IMRT is used instead of 3-dimensional conformal radiotherapy (3DCRT) during isotoxic radiotherapy planning for NSCLC?

Secondary Research Question: Which patient characteristics can be used to predict the need for IMRT in isotoxic radiotherapy planning for NSCLC?

Outcomes and Impact
The research questions above are novel, and they build upon knowledge established in the literature. They will provide a practical basis from which the international radiation oncology community can implement isotoxic radiotherapy practically and safely. Results from this study will contribute to:
- A general methodology for isotoxic dose escalation with or without IMRT,
- A selection method between IMRT and 3D CRT,
- An IMRT class solution for isotoxic lung radiotherapy,
- A dataset of prescription doses and Organ at Risk (OAR) Dose Volume Histogram (DVH) information that will inform treatment decision by enabling the prediction of the maximum dose escalation level for individual patients.

These outcomes will influence the methodology of any future clinical studies or randomised controlled trials. It provides a basis on which radiotherapy departments can carefully select patients for isotoxic IMRT planning for NSCLC and appropriately target resources. Results from this study will directly feed into a clinical pilot study of isotoxic radiotherapy within the investigator’s NHS Trust. This project will be a collaborative process between radiographers, physicists and clinicians to test the predictive nature of data supplied from this study. Local control, survival and toxicity will then be correlated with prescribed dose and OAR DVH data.

This study has the potential to change practice. Results would facilitate the successful implementation of isotoxic radiotherapy treatment. This could result in improved survival for a group of patients that have poor outcomes. Not all patients may need IMRT for isotoxic treatment, but the targeted use of IMRT has the potential to both reduce side effects and improve the therapeutic ratio within the patient cohort. This research will also allow planning radiographers to adequately advise clinicians on the benefits of selecting IMRT for isotoxic radiotherapy.

Review of the literature
Background
Local failure in patients with NSCLC is high and 2 year local control rates have been reported at around 20% (van Baardwijk A et al 2010). For locally advanced disease and inoperable disease, patients who are not able to tolerate concurrent chemoradiotherapy are offered sequential chemoradiotherapy or radiotherapy alone (Lim et al 2011). In this situation, evidence from dose escalation trials suggests that doses higher than the standard 60Gy in 30 daily fractions (or BED equivalent) can lead to greater local control and overall survival (Belberos JSA et al 2006, Kong F et al 2005, 2006, Adkison JB et al (2008)). However, delivering higher prescription doses can be limited by late toxicity caused by higher doses to the OAR such as the lung and spinal cord (Kong F et al 2006).

Radiotherapy prescriptions have traditionally been tailored for the entire NSCLC population in a one-size-fits-all manner (e.g. 60 Gy in 30 daily fractions). However, the achievable maximum dose in a NSCLC radiotherapy treatment varies from patient to patient depending upon the size and position of the tumour in relation to the OARs. As higher prescription doses are more difficult to achieve in some patients, the literature suggests that it may be beneficial to treat patients with isotoxic radiotherapy, which involves prescribing each patient the maximum dose possible limited solely by their individual OAR dose constraints. Recently, van Baardwijk et al (2010, 2008a, 2008b) have published the results of an ongoing study where total tumour dose was maximised to each NSCLC patient and limited only by OAR constraints to the spinal cord, lung, brachial plexus and main bronchi. This study resulted in the treatment of 166 patients treated with individualised prescriptions ranging from 51.9 Gy to 79.2 Gy in twice daily fractions of 1.8 Gy. The series showed similar survival rates to patients treated with concurrent chemoradiotherapy, and minimal toxicity. All patients were treated with a 3DCRT.

The Problem
Case series demonstrate improved clinical outcomes when IMRT is used instead of 3DCRT for...
References:


