Clinical Commissioning Policy Statement: Proton Beam Therapy for Lung Cancer (Adults)[201201P] (URN:1923)

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Commissioning position

Summary

Proton beam therapy is not recommended as a treatment option for patients with lung cancer (Adults).

Information about proton beam therapy

The intervention

Proton beam therapy (PBT) provides radiation by delivering a beam of proton particles rather than x-rays. The physical properties of protons results in a significantly reduced dose being deposited in the normal tissue beyond the tumour. This is in contrast to x-rays where there is dose extension beyond the tumour.

The treatment has some advantages over conventional radiotherapy in certain groups of patients, such as children, or where the cancer is close to a critical part of the body such as the spinal cord. However, for many groups of patients or types of cancer, including those with lung cancer, there is as yet little evidence of improved treatment outcomes, such as better cancer control or reduced side-effects, when compared to conventional photon-based radiotherapy treatment.

Committee discussion

Clinical Panel considered that the proposition reflected the evidence base presented and supported the not for routine commissioning position.

See the committee papers (link) for full details of the evidence.

The condition

Lung cancer is cancer that starts in the windpipe (trachea), the main airway (bronchus) or the lung tissue. It is the third most common cancer in the UK with 47,235 new lung cancer cases diagnosed annually between 2014-2016. The condition is highest in people aged 85-89 and is more common in people living in the most deprived areas of England. Lung cancer is the leading cause of cancer death in the UK, accounting for 21% of all cancer deaths in 2016. Only around 5% of lung cancer patients survive for 10 years or more.

There are two main forms of primary lung cancer. These are classified by the type of cells in which the cancer starts growing. They are:

- Non-small-cell lung cancer (NSCLC) – the most common form, accounting for more than 87% of cases. It can be one of three types: squamous cell carcinoma, adenocarcinoma or large-cell carcinoma.
- Small-cell lung cancer (SCLC) – a less common form that usually spreads faster than non-small-cell lung cancer.

The type of lung cancer you have determines which treatments are recommended.

Current treatments

There are a range of different treatments currently available in the treatment of lung cancer, including surgery, radiotherapy, chemotherapy, or a combination of all three. These treatments can be given either to cure the cancer or to manage symptoms and pain which is called palliation. The appropriate treatment for lung cancer depends on a range of factors, including its type, how far it has spread (determined by the stage) and the overall health and fitness of each individual patient.

Where primary lung cancer is diagnosed at an early stage and the overall health and fitness of an individual is good, surgery is the preferred first treatment, sometimes followed by chemotherapy. Where surgery isn't possible, and/or the cancer has spread too far, radiotherapy is usually the preferred treatment. Chemotherapy is usually only given as a first treatment for lung cancer in cases that are diagnosed at an advanced stage and where surgery and radiotherapy are not considered to be effective.

Where treatment with radiotherapy is required, there are a range of different types of radiotherapy available. In recent years, the introduction of newer radiotherapy techniques has led to a reduction in toxicity and the ability to safely treat patients with lager tumours or tumours that are near other organs with curative intent. These techniques include:

- Stereotactic ablative radiotherapy (SABR), whereby a higher dose of radiation is spread of smaller number of treatment sessions;
- Intensity modulated radiotherapy (IMRT), a type of radiotherapy whereby the radiation beam is shaped to closely fit the area of the cancer; and
- 4-dimensional radiotherapy, a radiotherapy technique which involves images being taken during the treatment. The radiotherapy machine then adjusts the position of the couch using the information from these images and treatment starts/stops based on a patient's breathing.

Comparators

External beam radiotherapy (photons) – including conventional radiotherapy, SABR, IMRT and 4D radiotherapy.

Clinical trial evidence

Evidence summary

NHS England has concluded that there is not sufficient evidence to support a policy for the routine commissioning of this treatment for the indication .Three papers were submitted to the Clinical Panel as part of the policy. One paper reported findings from a randomised trial, a second reported findings of a phase two clinical trial and a third reported a secondary analysis of a randomised trial. These papers did not provide persuasive evidence of the superior clinical effectiveness of proton beam radiotherapy over current standard treatment.

Paper 1. Liao Z et al (2018). Bayesian Adaptive Randomization Trial of Passive Scattering Proton Therapy and Intensity-Modulated Photo Radiotherapy for Locally Advanced Non-Small-Cell Lung Cancer. Journal of Clinical Oncology.

This randomised trial compared outcomes of passive scattering proton therapy (PSPT) versus intensity-modulated (photon) radiotherapy (IMRT), both with concurrent chemotherapy, for inoperable non-small-cell lung cancer (NSCLC). The primary outcomes of interest were first occurrence of grade greater than or equal to 3 radiation pneumonitis or local failure.

Eligible patients had stage II to IIIB NSCLC, or stage IV disease with a single brain metastasis, or a recurrent tumour after surgical resection amenable to chemoradiation; had a Karnofsky performance score of greater than or equal to 70, and baseline pulmonary function of forced expiratory volume in 1 second greater than or equal to 1 litre.

A total of 149 patients were randomised to receive either PSPT or IMRT with chemotherapy. The patients ranged in age from 33 to 85 years (median 66 years) and were followed up over 72 months. The median follow-up times for all patients were 24.1 months and 25.7 months in the IMRT and PSPT groups respectively.

At 1 year, radiation pneumonitis occurred in 8.1% of all patients (6.5% in the IMRT group; 10.5% in the PSPT group); corresponding occurrences of local treatment failure were 10.9% and 10.5% respectively. There were no statistically significant differences between the groups for either primary endpoint measure. Improvements in both measures were reported in both groups over the course of the trial, suggesting a learning curve associated with implementing PSPT.

Median overall survival was 29.5 months in the IMRT group and 26.1 months in the PSPT group, with no statistically significant difference between the groups.

The findings after six years of follow-up are insufficient to draw conclusions on the superiority of proton therapy over photon radiotherapy for locally advanced non-small-cell lung cancer.

Summary

This prospective randomised trial found no clinical benefit in grade 3 or higher radiation pneumonitis or local treatment failure, and no improvement in median survival following treatment with passive scattering proton therapy compared to photon for patients with locally advanced non-small-cell lung cancer.

Paper 2. Yang P et al (2018). Patterns of Local-Regional Failure After Intensity Modulated Radiation Therapy or Passive Scattering Proton Therapy with Concurrent Chemotherapy for Non-Small Cell Lung Cancer. International Journal of Radiation Oncology.

This paper reported findings of a secondary analysis of a randomised trial (described in paper 1) comparing IMRT and PSPT for locally advanced non-small cell lung cancer. In this study, the authors compared differences in patterns of locoregional treatment failure in patients who received each treatment.

In total, 212 patients with NSCLC who enrolled in a randomized trial of IMRT and PSPT were analysed. Treatment simulation computed tomography scans and dose distributions were registered with images depicting recurrence. Weekly during treatment 4-dimensional computed tomography simulation and verification plans were obtained for all patients.

The key result in this paper was that there were no statistically significant differences in rates of marginal failure between the groups (12% among IMRT patients and 9% among PSPT patients). The authors concluded there were no differences in patterns of local, marginal, or regional failure between patients treated with IMRT or PSPT.

In summary, this study reported comparable treatment failure rates between proton therapy and photon therapy.

Paper 3. Chang JY et al (2017). Proton Beam Radiotherapy and Concurrent Chemotherapy for Unresectable Stage III Non-Small Cell Lung Cancer: Final Results of a Phase 2 Study. JAMA Oncology.

This paper reports findings of an open-label, single group assignment phase 2 study evaluating high dose proton beam radiotherapy (PBT) with concurrent chemotherapy to treat unresectable stage III Non-Small Cell Lung Cancer (NSCLC). The primary outcome measure was overall survival; other outcome measures of interest were progression-free survival, distant metastasis and recurrence. Other key outcomes to be evaluated were acute and late toxic effects.

Eligible patients had inoperable, stage III, histologically or cytologically confirmed NSCLC, Karnofsky performance status 70 to 100 and 6-month pre-diagnosis weight loss of no more than 10%.

A total of 84 patients were enrolled to receive the intervention (PBT with concurrent chemotherapy) and 64 were included in the analysis. The patients ranged in age from 37 to 78 years (median 70 years); median follow-up was 27.3 months for all patients and 79.6 months for survivors.

Median overall survival was 26.5 months and 29% at 5 years (95% CI 18-41%). Median progression-free survival was 12.9 months, with five-year progression-free survival of 22% (95% CI 12-32%). Five-year actuarial distant metastasis and locoregional recurrence were 54% and 28% respectively. Low rates of toxicity were reported in both the acute and late settings, relative to historical data with photon-based therapy.

The usefulness of the study for evaluating the clinical effectiveness of PBT as an intervention in locally advanced NSCLC was limited by the absence of a comparator or control group; the authors identified the need for future multi-institutional prospective trials to address this evidence gap. The findings are therefore insufficient to draw conclusions on the superior effectiveness of proton therapy relative to photon radiotherapy for treatment of locally advanced non-small cell lung cancer.

Adverse events

Adverse events were not demonstrated in the literature provided.

Policy review date

This is a policy statement, which means that the full process of policy production has been abridged: a full independent evidence review has not been conducted; and public consultation has not been undertaken. If a review is needed due to a new evidence base then a new Preliminary Policy Proposal needs to be submitted by contacting england.CET@nhs.net.

Links to other policies

Not applicable.

Equality statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities