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ORIGINAL ARTICLE

The potential of proton beam radiation for palliation and reirradiation

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Abstract

A group of Swedish oncologists and hospital physicists have estimated the number of patients in Sweden suitable for proton beam therapy. The estimations have been based on current statistics of tumour incidence, number of patients potentially eligible for radiation treatment, scientific support from clinical trials and model dose planning studies and knowledge of the dose-response relations of different tumours and normal tissues. If an estimated 1% of the palliative treatments can be administered by protons with substantial benefits to the patient, almost 100 patients per year in Sweden would be eligible. It is further estimated that around 150 patients per year in need of reirradiation would benefit from radiation with protons compared to photons.

Radiation for palliation

Palliative radiation therapy is a thoroughly studied and evidence-based treatment modality for most of the symptoms accompanying incurable malignancy. Pain due to skeletal metastasis is one common indication for palliative radiotherapy with a reported response rate of 75–100% [1]. Spinal compression [2], dyspnoea [3], neurological symptoms due to brain metastases [4], haemorrhage [5] and compression of the great thoracic vessels [6] are other specific and common symptoms in cases of disseminated malignancy which palliative radiotherapy may alleviate. A local recurrence, wherever it occurs, is frequently associated with severe symptoms, and represents a therapeutic challenge.

The Swedish Council on Technology Assessment in Health Care (SBU) report on radiotherapy for cancer states that about 45% of the radiotherapy administered in Sweden is given for palliation, i.e. with the intention of alleviating the patient's illness-induced symptoms without causing treatment-induced symptoms, thus improving the patient's quality of life [7]. This is usually achieved by administering a lower radiation dose than will cause a symptomatic acute reaction in normal tissues. This obviously leads to a relatively low dose being

administered to the tumour tissue as well and thus to less decrease in tumour mass than if a higher dose had been given locally. Tumours for which effective systemic treatments exist, for instance hormonal treatment of breast and prostate cancer, are often associated with relatively long survival, even in cases of disseminated disease [8–12]. In these types of tumours, it is often desirable to achieve pronounced tumour reduction with a high radiation dose in order to gain complete control of symptoms and avoid local progression as long as the patient responds to hormonal or other maintenance treatment. Another situation in which palliative high-dose radiotherapy may be required is in rapidly growing tumours [13].

Clinical experience of proton therapy in palliative radiotherapy

Proton therapy might be one way of concentrating a high radiation dose to a tumour area without evoking severe symptoms in normal tissues. There are, however, no reports in medical scientific publications concerning clinical experience of protons for palliation of symptoms in cases of disseminated malignancy, which does not unequivocally mean that no such experience exists.

Assessment of the number of proton therapy cases

It is difficult to estimate the number of patients annually in Sweden for whom protons would be significantly better than three-dimensional conformal radiotherapy (3D-CRT), since this figure is affected by expected survival, the patient's total tumour burden, the patient's functional condition, the possibility of symptom alleviation with other treatments and the amount of time spent away from home during the therapy. According to the above-mentioned SBU report, about 8 300 palliative series were administered yearly in Sweden. If an estimated 1% of the palliative treatments could be administered by protons with substantial benefits to the patient, almost 100 patients per year in Sweden would be eligible.

Summary assessment

An estimated 100 patients in need of radiation therapy for palliation could be offered better alleviation of their symptoms with proton therapy, if it were available in Sweden. The potential benefits of this treatment are reduced acute side effects, and thus the possibility of improved quality of life.

Reirradiation

The possibility of reirradiating a residual or recurrent tumour is always limited by the previously given radiation dose, the normal tissue tolerance, surrounding critical organs, and of the time elapsed since the first radiation treatment. External reirradiation is mostly delivered with as small a margin as possible. In order to gain treatment time, higher doses per fraction is often used. Sometimes reirradiation is performed with intracavitary or interstitial brachytherapy, in order to limit the treated volume. The adverse effects are related to the involved and surrounding normal tissues and this often heavily restrict the dose.

Clinical experience of proton therapy

Reirradiation of 16 patients with nasopharyngeal carcinoma is reported on from the proton therapy centre in Loma Linda, California, USA. Doses around 60–70 Gy were given with protons without serious side-effects and with 50% two years survival [14].

Model studies

There are no simulation studies done concerning reirradiation. But extrapolation of results from other simulations shows that higher tumour doses could be

given with lower doses to normal tissues and critical organs. For example, in a comparative dose planning study, Goodman et al. [15] addressed the problematic issue of repeat radiotherapy in patients with recurrent malignant lymphoma involving the mediastinum. It was found that IMRT using photons resulted in improved possibilities to deliver an adequate dose to the lymphoma compared to 3D-CRT. Further improvements seem likely using protons.

Calculations of the number of cases for reirradiation with protons

All patients in need of reirradiation can potentially benefit from proton treatments compared to photon treatments. One hundred to 150 patients per year seem plausible. This is based upon an estimate that 10% of all curatively irradiated patients have a local failure and that 10–15% of those need reirradiation.

Need for research

No trials having been carried out comparing photons and protons in reirradiation, it is highly recommended that such trials be initiated. Since the group of patients is very heterogeneous, randomized trials will be very difficult to perform.

Summary assessment

It is estimated that around 150 patients per year in need of reirradiation would benefit from radiation with protons compared to photons. The chances of local control would increase and the adverse effects decrease.

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