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Short Commentary

Using a Robotic Stereotactic Radiation Treatment System for Re-Irradiation may be Safe and Effective

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Background

With the advent of systematic treatment cancer patients are living longer. This has led to an increase in the number of local recurrences facing radiation oncologists. Among the salvage treatment strategies, re-irradiation has been used successfully [1-3] in addition to salvage chemotherapy and surgery [1,3]. The use of re-irradiation is limited because there is a substantial risk of re-irradiation to critical normal tissues [2]. Recent technological advance in stereotactic radiation treatment systems [2] has allowed safer and more effective use of re-irradiation. Among many other factors that may have contributed to the improvement of re-irradiation outcome, this paper limits its scope focusing on the key issues facing re-irradiation:

1. Determining which patient should be treated with re-irradiation.

2. The dose and schedule of re-irradiation and when to treat.

3. The expected outcome and toxicity, and how to improve the outcome using the capacities of modern radiation treatment systems.

Current status of re-irradiation of recurrent cancers

The major sites of re-treatment are brain metastasis [4], spinal metastasis[5], recurrent head and neck cancers [6], lung cancers[7], livercancers [8], and abdominal and pelvic cancers[9]. The major advancement in modern radiation treatment machines includes the ability of the machines to identify anatomical landmarks or fiducial markers and track them accurately and efficiently with on-board imaging.This stereotaxy may improve the outcomes and limit the toxicities. For example, cyberknife (Accuray Inc., Sunnyvale, CA) robotic stereotactic radiation system [10] uses skull tracking, Xsightspine tracking, XSight lung tracking for peripheral lesions, implanted fiducial tracking, and Synchrony real-time tracking system. With the many degreesof freedom of the robotic arm, it could deliver very high dose efficiently and safely with activetracking. Other advanced systems may have similar capacities also [11-13].

Treatment planning

The definition of the salvage target volume is different from those used in the initial treatment, with a margin that may be tighter as needed. PET scan may be useful in defining the gross tumor volume (GTV) and clinical target volume(CTV) [14]. For example, the cyberknife treatment planning computer system allows multi-modal image registration including CT to MRI and CT to PET image registration. This would allow more accurate target delineation. The cyberknife system uses robotic arm to go through a large number of nodes (positions) to optimize the dose distribution. Hypofractionated stereotactic radiotherapy is well suited for re-irradiation because of its high precision.

Discussion

The outcome and toxicity are generally better in

re-irradiation with more advanced stereotactic machines. For example, cyberknife has become well recognized to be useful in radiation re-treatment because of its robotic stereotaxy. The results of cyberknife re-treatment are encouraging in both salvage rates and toxicity rates. Other advanced stereotactic radiation systems also produce encouraging results when used in re-irradiation[11-13].

Patient selection may include cancer control elsewhere, expected life expectancy, the condition of the critical structures, and time to radiation [15,16]. The normal tissue tolerance may be different than that of initial course of radiotherapy [2,17,18]. To find the combined effects of different doses and fractions between the initial radiotherapy and re-irradiation, Biologic Effective Dose (BED) and Biologic Equivalent Dose at 2 Gy per fraction (EQD2)[19]may be calculated, and the dosimetric guidelines may be applied. However, tumor control and normal tissue tolerance data based on actual re-irradiation clinical experience are scant [1,2,11,20].

A clinical example

A hypothetical 55 years old man,with a Karnofski performance score (KPS) of 90, has a non-small cell lung cancer treated with definitive chemoradiation to the chest to 63 Gy in 1.8 Gy fractions and whole brain treated to 30 Gy in 10 fractions one year ago. Now he has recurring 3cm hilar lymphadenopathy and a progressive 2cm brain metastasis. What is the salvage radiation treatment strategy supported by the literature [7,21,22]?

The prognostic value of KPS has consistently been found to be important in selecting which patients will benefit from re-irradiation[2,23]. This patient would have a high probability of benefitting from the re-irradiation. The Biologic Effective Dose (BED) less than 150 Gy has been found to be effective and safe for 3 cm or less recurrent non-small cell lung cancer [24]. For the brain lesion, it could be treated with stereotactic radiosurgery (SRS). In initial stereotactic radiotherapy of brain metastasis, this margin could be as small as 0-2mm [25]. The SRS could be fractionated to improve the tolerability of the re-irradiation. Unlike initial treatment, there is no well accepted dosimetric guidelines for normal tissue tolerance in re-irradiation [2]. However, the Quantec guidelines [18] and Task Group 101 report [17] may be useful in helping to select the optimal dose for the treatment. In this case, the critical structures are the spinal cord, trachea, bronchi, great vessels, chest wall and esophagus. A list of the Biologic Equivalent Dose at 2 Gy (EQD2)[19] could be calculated for each of these critical organs, the tolerance of these structures could be estimated in the literature[1,2]. The tolerance dose levels could then be adjusted according to the toxicity tolerance based on the performance status and desire of the patient. For example, a hypothetical 5-10% risk of normal tissue toxicity may be acceptable to some patients in the re-irradiation setting as opposed to the 0-5% risk in the initial treatment setting.

Re-irradiation using advanced radiation treatment systems such as cyberknife may be effective and safe. It should be considered among the salvage strategies.

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