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Development of radiotherapy for liver cancer

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Abstract

Radiotherapy for liver cancers used to be palliative treatment. Currently, three-dimensional conformal radiotherapy, stereotactic body radiotherapy, and particle beam therapy using proton beams and carbon ion beams are used for the treatment of liver cancers. Radiotherapy for liver cancers has become to curative treatment due to the various technical progress. Radiotherapy can accomplish safe and effective treatment for liver cancers.

Introduction

Accurate localized diagnosis of liver cancers was difficult until the 1970s, and significance of radiotherapy for liver cancers is only palliative because it was difficult to suppress the damage to the radiosensitive liver. However, as Computed Tomography (CT) became widespread for treatment planning in the1980s, the localized diagnosis of lesions became easy, therefore, treatment could be performed while reducing liver damage. In recent years, radiotherapy is recognized to be one of the curative treatment technique for liver cancers. Here we outline contemporary liver cancer radiotherapy.

Three-dimensional conformal radiotherapy (3D-CRT)

X-rays are usually used in 3D-CRT. Radiation is beamed from a direction perpendicular to the body axis in most cases; however it can be delivered from other directions by turning the patients' bed. One advantage of 3D-CRT is that it means the shape of the irradiation field can be set 3-dimensionallyenablingdelivery of enough radiation to the target, accomplishing conformal beam irradiation to the target, while suppressing the irradiation dose to important tissue around the tumor. 3D-CRT is used in cases when other treatments are not available due to Portal Vein Tumor Thrombosis (PVTT), unrespectability, or some complications.

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A total irradiation dose around 45-50 Gyat a daily dose of 2 Gyisoften reported. There have been many prospective studies in which the response rate was30-80% and the 1-year survival rate was 25-50% for PVTT or for Inferior Vena Cava Thrombosis (IVCT) patients [1-4]. Prospective and retrospective studies of unrespectable cases have shown that the survival of patients who received Transarterial Chemoembolization (TACE) with radiotherapy was longer than patients who received only TACE, and a meta-analysis study also proved higher response and survival rates in the TACE-with-radiotherapy group[5].As for adverse effects, it has been reported that radiotherapy can be performed safely, with only elevation of the total bilirubin value in many cases [5].

Stereotactic body radiotherapy (SBRT)

SBRT has a feature for treating small tumors. To condense radiation and to hit the target accurately, it meets 3 criteria: ① higher dose to be delivered to a small target in a short term from multiple directions using a linear accelerator, ② geometrical accuracy finer than 5mm in every treatment session, ③ immobilizing the patient in position and countermeasures for respiratory movement. Various device to fix the body and highly accurate position matching system are required.

A total dose of 30-50 Gy at a daily dose of 6-15 Gy to the tumor less than 5cm is usually performed. Even when the lesions treated are difficult to cure by other local treatment, relatively good outcomes are reported, such as a response rate of 50-85%, 1-year local control rate of 65-100%, 1-year overall survival rate 50-90%, 2-year local control rate of 90-95% [6-10]. Serious liver damage from the technique is very rare.

Particle beam therapy

Particle beam therapy uses high-energy protons carbon ions. In contrast to X-rays, accelerated charged protons and carbon ions release their maximum energy just before they stop, creating a steep peak of energy called the Bragg-peak. Furthermore, regulating the dose distribution in the depth direction can be accomplished by mixing different energy beams together, called the spread-out Bragg peak. Figure 1 shows the concepts of X-rays and particle beams and Figure 2 shows dose distribution of proton beam therapy for liver cancers. Although the indication for treatment is similar to X-ray radiotherapy, particle beam therapy can treat more advanced disease condition.

There are many reports of a total dose of radioactivity 60-70 Gray Equivalent (GyE) at a daily dose of 2-6 GyE for proton beam therapy. Dose escalation studies of carbon ion beam therapy from 49.5 GyE to 79.5 GyE reveal that a total dose of 72 GyE at a daily dose of 4.8 GyEis ideal [11], and short term treatment protocols, such as approximately 50 GyE in 1-2 weeks, is also done. Many previous studies treated patients in Child-Pugh classification A or B whom it was difficult to give other local treatment [12-15,16]. In addition, PVTT, IVCT or a huge tumor can be applied [17,18]. Excellent local control with extremely rare adverse effects can be achieved.

Conclusion

Radiotherapy for liver cancer has been developed due to technical progress such as the improvement of imaging, three-dimensional treatment planning, reproducible irradiation technique, and precise management of the irradiation treatment system. In the daily clinic, more number of patients has come to hospital to ask for radiotherapy.

On the other hand, clinical history of radiotherapy for liver cancer is at most 20-30 years. Thus, there is still no firm consensus about indications for this treatment. Although there are many reports about effectiveness and safety, they do not refer to evidence-rich data for deciding the criteria for radiotherapy. More evidence-rich data is required in order to popularize radiotherapy for liver cancer to help these patients in future.

Figures

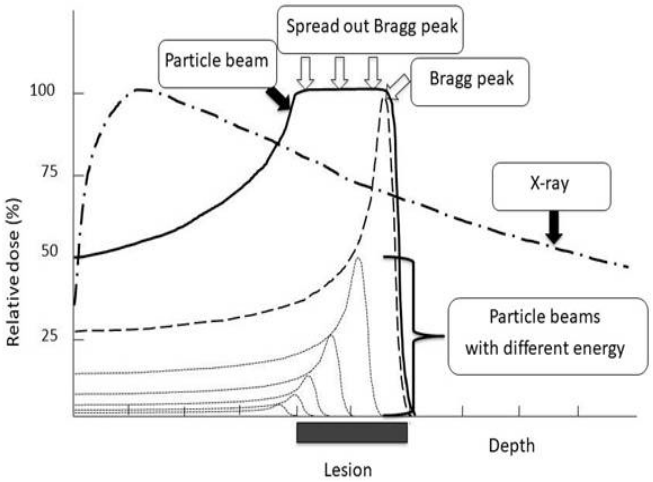

Figure 1: Relative dose and depth (comparison of X-rays and particle beams).

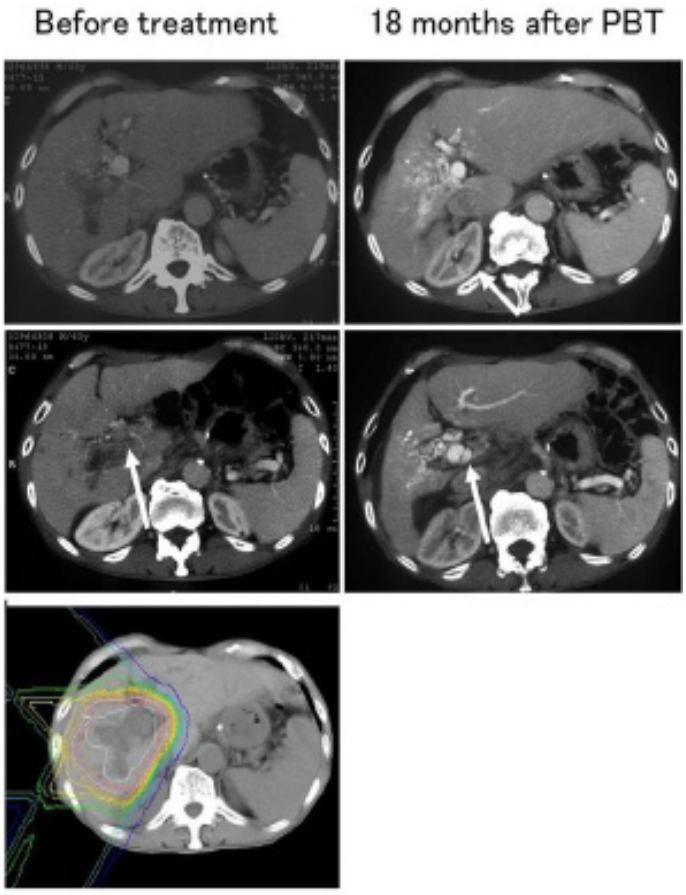

Figure 2: HCC patient. 63 years old man having HCC with PVTT (Vp4). Complete response and re-canalization was seen 18 months after PBT (arrow).

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