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Stereotactic body radiation therapy for primary and metastatic liver tumors: From technological evolution to improved patient care

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A B S T R A C T

Technical developments allowed stereotactic body radiation therapy (SBRT) to deliver effective doses of irradiation with high precision in a small number of fractions. This paper reviews the role of SBRT for liver metastases, hepatocellular carcinoma and cholangiocarcinoma, paying special attention to patient eligibility and treatment outcomes regarding local control, toxicity and quality of life. As well as discussing specific issues of these different tumors, such as the presence of underlying liver cirrhosis and the impact on toxicity, it outlines the limitations of SBRT and future areas of development and research.

Introduction

The role of radiotherapy in the treatment of liver tumors has been limited. This is due to the evidence that conventional radiation treatments could treat the whole liver safely only up to doses that led to palliation of symptoms [1,2]. Technical developments in the 1980s and 1990s made it possible to deliver high radiation doses to limited volumes of the liver, producing promising results with regard to

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local control and toxicity [3,4]. Methods that use a small number of fractions with a high degree of precision to deliver a high dose of radiotherapy to a target in the body are now referred to as stereotactic body radiation therapy (SBRT) [5]. This technique creates a sharp fall-off in dose between the tumor and the normal tissues surrounding it. For primary and metastatic liver tumors, this treatment option is generally offered as an ablative radical local treatment (Fig. 1). To correct for the variations in tumor position caused by respiration and for day-to-day-variations, technical advances for implementing stereotactic treatments have been introduced such as image-guided radiotherapy, i.e. frequent imaging during treatment (Fig. 2).

Although the mechanism of radiation-induced cell death is known to be caused predominantly by radiation-induced DNA damage or breaks, the use of highly concentrated stereotactic treatments may be accompanied by other mechanisms, such as indirect cell death caused by vascular damage [6].

This paper reviews the role of SBRT for liver metastases, hepatocellular carcinoma and cholangiocarcinoma. As well as presenting patient eligibility criteria and treatment outcomes, we also outline the limitations of this technique, examine technical developments and discuss current and future areas of research.

Liver metastases

Patients with liver metastases referred for SBRT are those who are ineligible for surgery and are often ineligible for radiofrequency ablation (RFA) [7–12]. This is because the effectiveness of SBRT is not impaired by the blood flow in the vessels or the bile accumulated in the gallbladder. It is also the case that external radiotherapy is not subject to restrictions on reaching any tumor location in the liver, such as the sub-diaphragmatic region, which may be more difficult to approach with RFA.

The largest group of patients treated with SBRT consists of patients with liver metastases from primary colorectal cancer. Nevertheless, many studies have also included metastases from other primaries such as breast, non-small-cell lung cancer, ovary, and melanoma [7,10,13–15]. Ideally, if extrahepatic disease is present in these patients, it should be limited and potentially treatable [7,8,13,15,16]. A Karnosfky performance status $\geq$70% or an ECOG scale $\leq$2 is often recommended [7,8,10,14,16].

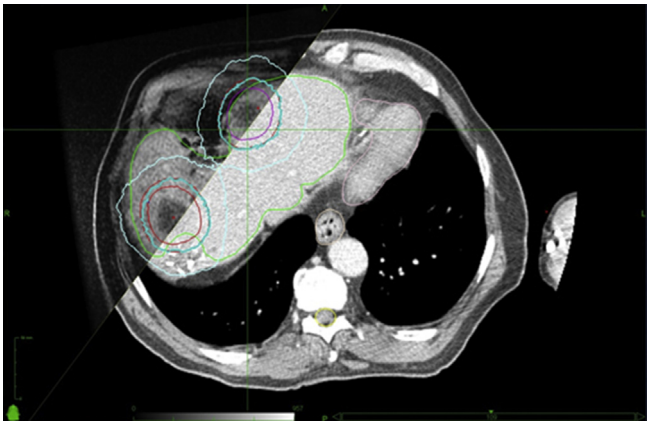

Fig. 1. Dose distribution corresponding to a patient treated with SBRT due to two liver metastases from primary colorectal cancer. This patient underwent earlier surgery and several RFA treatments. CT planning was combined (fused) with MRI. Metastases were delineated in red and pink. The margin surrounding the tumor to compensate for breathing motion and daily uncertainties is shown in red. The turquoise line represents the dose prescribed (60 Gy delivered in eight fractions), and the light blue line represents the 30 Gy area. The liver is contoured in green. Previous RFA areas are not included in the normal liver volume. Heart, esophagus, spinal cord, stomach, duodenum, lungs and kidneys have been delineated and were taken into account for the volumetric dose calculations.