



## Critical Review

# Hepatocellular Carcinoma Radiation Therapy: Review of Evidence and Future Opportunities

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Hepatocellular carcinoma (HCC) is a leading cause of global cancer death. Curative therapy is not an option for most patients, often because of underlying liver disease. Experience in radiation therapy (RT) for HCC is rapidly increasing. Conformal RT can deliver tumoricidal doses to focal HCC with low rates of toxicity and sustained local control in HCC unsuitable for other locoregional treatments. Stereotactic body RT and particle therapy have been used with long-term control in early HCC or as a bridge to liver transplant. RT has also been effective in treating HCC with portal venous thrombosis. Patients with impaired liver function and extensive disease are at increased risk of toxicity and recurrence. More research on how to combine RT with other standard and novel therapies is warranted. Randomized trials are also needed before RT will be generally accepted as a treatment option for HCC. This review discusses the current state of the literature and opportunities for future research. © 2013 Elsevier Inc.

## Introduction

Primary liver cancer is the world's third most common cause of cancer death (1). Eighty-five percent of cases occur in developing countries, and it is the fastest growing cause of cancer death in the United States (2). Hepatocellular carcinoma (HCC), the focus of this review, accounts for 85%-90% of primary liver cancers.

Risk factors for HCC include hepatitis B, hepatitis C, alcohol ingestion, and cirrhosis from any cause. Patients with HCC are often asymptomatic at the time of diagnosis, with a liver lesion incidentally detected via imaging. Classic imaging characteristics of arterial-phase enhancement and venous-phase "washout" in high risk patients with lesions >2 cm are diagnostic for HCC even without a biopsy (3). Many HCC staging systems have been developed, and most are based on the extent of tumor and vascular invasion (4). Figure 1 illustrates the Barcelona Clinic Liver Cancer system, which incorporates tumor stage, liver function, and performance status to facilitate treatment decisions (5).

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In this review, the role of external beam radiation therapy (RT) for HCC will be summarized, and opportunities for future research highlighted. Percutaneous brachytherapy and radio-embolization have also been used to treat HCC, but are not the focus of the present review.

## General Treatment Overview

HCC tends to remain within the liver, although multifocality and vascular invasion (eg, to the portal vein) are common (6). The common presence of underlying liver disease increases the risks of all HCC therapies compared with liver metastases occurring in a noncirrhotic liver. Cure with preserved liver function is an overall treatment goal, and liver function is an important component of treatment decisions.

Surgical resection, an option for the minority of tumors, results in 5-year survival rates of 60%-70% (5, 7). Liver transplantation can cure both the cancer and underlying liver disease. Four-year survival

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