

CyberKnife SBRT Treatments Prove Effective for Liver Cancer

Hepatocellular carcinoma (HCC) accounts for most liver cancers, and often results from primary risk factors such as Hepatitis B, Hepatitis C and cirrhosis. HCC is the 8th most common solid tumor in the world, with about 1 million new cases, and 400,000 deaths per year. However, the incidence in the United States is low, at one to three per 100,000.

Historically, surgery has been the most effective treatment for HCC, with a five-year survival rate of 50 percent to 70 percent for Stage I, 30 percent to 50 percent for Stage II, 10 percent to 30 percent for Stage III, and 10 percent for Stage IV. The most aggressive surgery is a total hepatectomy plus liver transplant, which has significantly lower five-year survival rates of between 20 percent and 45 percent.

Chemotherapy (CT) – which includes use of agents such as Cisplatin, Adriamycin, 5-FU, Etoposide, Paclitaxel, and Mitoxantrone – has not been shown to be effective in treating HCC. The response rate is in the range of 10 percent to 20 percent. However, when combined with external beam radiation therapy (XRT), the response rates improve (see chart below).

UNRESECTABLE HCC RESPONSE RATE TO XRT +/- CT					
AUTHOR		#PTS		DOSE-Gy	RESPONSE
Stillwagon		194		21	22%
Order		105		21	48%
Seong		27		52	67%
Dawson		25		59	68%
Guo		76		nr	47%
Seong		158		48	67%
Kim		54		45	42%
Huang		41		51	81%

Trans-catheter Arterial Chemoembolization (TACE) also has been combined with XRT in unresectable HCC with varying degrees of success (see chart below):

UNRESECTABLE HCC TACE + XRT THREE-YEAR SURVIVAL			
AUTHOR	#PTS	SURVIVAL	
Guo	107	28%	
Cheng	17	58%	
Yasuda	44	81%	
Seong	158	22%	
Wu	42	78%	

The limiting factor of this combined treatment is the tolerance of the liver to XRT, which depends on dose and volume of liver irradiated. The whole liver can tolerate ~ 35 Gy in conventional fractionation (1.8 Gy per day). It is important to note, though, that this is only a palliative XRT dose. Small volumes of the liver can receive 50 Gy to 60 Gy without long-term morbidity. In patients with unresectable HCC, the combination of XRT + CT, is a reasonable option, for both palliation and extending survival. Consider the results (below) in a study HCC patients treated with XRT + CT.

UNRESECTABLE HEPATOMA SURVIVAL AFTER XRT + CT				
#PATIENTS	MONTHS	1-YR	2-YR	
76	7.6	39%	11%	

**Source: Abrams et al, from Johns Hopkins, (IJROBP, 1994 ; 30)*

In recent years, the advent of conformal radiation treatment delivery systems, such as the CyberKnife System, which delivers stereotactic body radiation therapy (SBRT) and intensity modulated radiation therapy (IMRT) are showing promise in treating HCC. SBRT and IMRT enables contoured radiation dosimetry, which maximize the radiation delivered to the tumor while minimizing the exposure of normal surrounding tissues and organs.

While IMRT and SBRT virtually duplicate Gamma Knife dosimetry, both have an advantage over Gamma Knife in that they can be given anywhere in the body. In addition, IMRT and SBRT can take advantage of fractionated radiation delivery, which maximizes sparing of normal tissues. As a result, the IMRT and SBRT enables higher radiation dose to the tumor, and decreased exposure to normal tissue. These advantages are expected to result in better tumor control, improved long-term survival, and fewer complications.

SBRT has been used in the treatment of HCC, as shown in the chart below. It should be noted that most of these patients were not surgical candidates, nor had they progressed after medical treatments. These results compare favorably to surgery. Radiation dose regimens ranged from 42 Gy to 60 Gy in three to five fractions. Based on these results, SBRT has been judged to be safe and effective non-invasive treatment option for patients with HCC \leq 6 cm and Child-Turcotte-Pugh's Class A or B.

HCC RESULTS WITH SBRT					
		OVERALL	LOCAL		GRADE 3-4
AUTHOR	#PTS	SURVIVAL	RECURRENCE	F/U	COMPLICATIONS
Cardenas	17	60%	0%	2 yrs	0%
Kang	50	69%	5%	2 yrs	10%
Huang	36	64%	25%	2 yrs	0%
Ibarra	32	55%	44%	2 yrs	9%
Seo	38	61%	34%	2 yrs	3%
Andolino	60	67%	10%	2 yrs	13%
Kwon	42	59%	32%	3 yrs	2%
Huertas	77	57%	1%	2 yrs	23%
Scorsetti	43	45%	36%	2 yrs	16%
Jang	108	67%	13%	2 yrs	5%
Bibault	75	50%	10%	2 yrs	nr
Nouhaud	14	83%	22%	2 yrs	7%
Kang	50	69%	5%	2 yrs	11%
Yamashita	79	53%	nr	2 yrs	0%
Dewas	120	nr	25%	2 yrs	nr
Takeda	63	73%	8%	3 yrs	13%
Kimura	65	76%	0%	2 yrs	23%
Sanuki	185	70%	9%	3 yrs	13%
Yoon	93	54%	8%	3 yrs	7%

The CyberKnife System has been shown to be the SBRT delivery system providing the tightest radiation dose delivery. As a result, the CyberKnife System enables clinicians to give the maximum dose to the tumor target while minimizing dose to surrounding normal tissues.

The non-invasive, non-surgical nature of the CyberKnife System, treatments are often preferred for patients who have other health concerns and cannot undergo surgery. CyberKnife treatments are given daily for up to five days, on an outpatient basis. The treatments are painless and each session takes only about 45 minutes to deliver, resulting in fewer complications and minimal side effects when compared to other liver cancer treatment options.