

protocol for cyberknife®  
treatment of limited liver metastases

PROTOCOL LIVER

stereotactic body radiation  
therapy for liver

**ILLINOIS CYBERKNIFE®**  
AT ADVOCATE LUTHERAN GENERAL HOSPITAL





*CyberKnife delivers targeted, concentrated beams of radiation.*

## **Treatment Modalities**

Conventional radiation therapy has a limited role in the treatment of patients with liver metastases because the radiation doses are limited by hepatic parenchyma toxicity. The use of hypofractionated CyberKnife stereotactic therapeutic radiation entails a therapeutic radiation process that uses a more precise targeting methodology, allowing more focal treatment delivery to the tumor volume. CyberKnife more effectively limits the volume of adjacent tissue receiving high dose radiation which in turn allows the delivery of a much shorter series of treatments while employing a much larger dose of radiation per treatment. The radiation becomes tissue ablative within the high dose zone and as such, may be described as a form of radiosurgery.

## Efficacy

Until recently, liver metastases were thought to represent an incurable state, warranting palliative care only. It is now recognized that selected patients with a small number of metastasis (oligometastasis) may have curative outcome or delayed progression of disease with aggressive local therapy when combined with effective systemic therapy to address occult disease.

CyberKnife® stereotactic body radiation therapy (SBRT) has been explored in the treatment of liver tumors. CyberKnife can deliver potentially ablative doses of radiation therapy to a tumor with great precision and thus cause less damage to surrounding normal tissues, while yielding a higher radiobiologic effect on the tumor.

Although limited experience has been gained to date, the CyberKnife SBRT approach carries with it a number of potential advantages including the possibility of lower morbidity due to the very small treatment margins, more rapid recovery as SBRT is noninvasive and convenience of a few day treatment course.

## Protocol for CyberKnife SBRT of limited liver metastases

Prospective evaluation of low-dose irinotecan and the Cyberknife (SBRT) in the treatment of patients with colorectal cancer and limited liver metastasis.<sup>1</sup>

The purpose of the study is to explore the use of CyberKnife SBRT in conjunction with irinotecan in patients with fewer than four hepatic metastases who are not candidates for hepatic resection with the following endpoints:

- Determine toxicities of concurrent SBRT with concurrent irinotecan in patients with colorectal cancer and fewer than 4 hepatic metastases.
- Assess the tumor response rate in these patients
- Determine the progression-free survival and overall survival

## Schema



\*CyberKnife SBRT to liver metastasis 18Gy x 3

\*Per investigator decision and patient discussion, with consideration of age, performance, status, medical co-morbidities.

Irinotecan will be administered on the same day prior to SBRT treatment

## Suggested Inclusion and Exclusion Criteria

### Inclusion Criteria

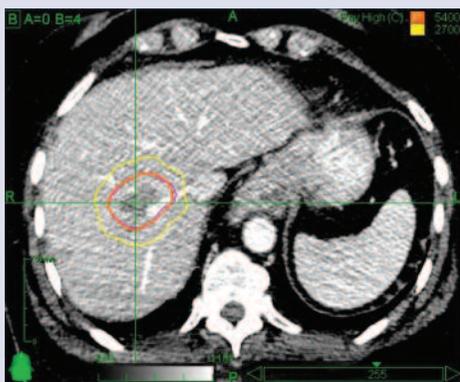
- Patient must be over the age of 18 years
- Histologically confirmed primary colorectal cancer
- Stage IV colorectal cancer with up to four liver metastases
- No additional sites of metastasis
- No malignant ascites
- At least 4 weeks from any chemotherapy
- No prior liver radiation therapy
- ECOG performance status 0-1

### Pretreatment Evaluation

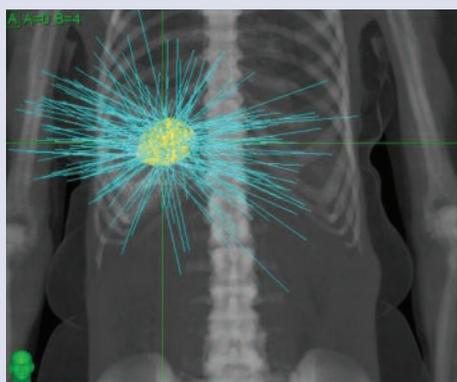
- Complete history and physical examination within 30 days prior to enrollment
- All patients will undergo abdominal CT or MRI with contrast 30 days prior to enrollment and a PET scan within 21 days of enrollment.
- Blood workup consisting of CBC with differential, complete metabolic profile and liver function tests.

### Treatment

- Irinotecan 40 mg/m<sup>2</sup> administered intravenously daily for 3 days (3 treatments within 8 elapsed days) prior to SBRT treatment.
- A minimum of three fiducial markers placed in the liver at least 1 week prior to treatment planning
- CT treatment planning scan performed more than 5 days post fiducial placement.
- The prescription dose of 54 Gy in 3 fractions shall be delivered in  $\leq 8$  days with  $\geq 95\%$  to the planning tumor volume (PTV).



The sub-millimeter accuracy of the CyberKnife ensures protection of surrounding critical structures.



Targeted angles creating a highly conformal 3D radiosurgical treatment.

## Assessment of Therapeutic Response

- Response to overall therapy will be based on the combined imaging studies of abdominal MRI/CT and PET scans
- One objective of this study is to define the "response rate" which is predicted at greater than 60%
- A second objective is to define toxicities. In the event Grade 3 or 4 toxicities exceed 50% among the first 20 patients the study will terminate.
- Investigators expect that 60%+/-0.15 with a confidence level of 95% of patients will have a "response" defined as CR+PR+SD, therefore the required sample size of 41 is necessary (Hully SB, Cummings SR, Designing Clinical Research. Williams and Walkins, Baltimore, MD 1988. Table 13.E.pg 220)

## The use of CyberKnife® hypo fractionated stereotactic therapeutic radiation

The CyberKnife is a unique noninvasive radiosurgical system, capable of treating any part of the body from any of approximately 1600 different targeting angles creating a highly conformal three-dimensional radiosurgical treatment volume, guided by orthogonal X-ray-based targeting feedback and delivering radiation by a highly collimated, robotically controlled linear accelerator.

The CyberKnife system targets implanted fiducial markers in the liver with sub-millimeter accuracy. The technology allows for real-time tracking and detection of liver tumor motion adjusting for this movement during the treatment delivery.

The feasibility of using CyberKnife for treating liver metastasis has been reported by a number of investigators. The results of these studies suggest that SBRT delivered without chemotherapy can result in control rates to the site of treatment up to 95%, depending upon the size of the tumors and the doses of radiation utilized.<sup>2</sup>

Chemotherapy delivered with radiation therapy may increase the effectiveness of treatment and may allow for a lower dose of radiation therapy to be utilized thereby limiting the negative side effects.

1 Hirsch A, Ruffer J, Sweeney P, Mohiuddin, M, Bitran J, Simon A., *Prospective Evaluation of Low-Dose Irinotecan and CyberKnife Stereotactic Body Radiotherapy in the Treatment of Patients with Colorectal Cancer and Limited Liver Metastasis.* 2013

2 Rusthoven KE, Kavanagh BD, CArdenes H, Stieber VW, Burri SH, Geigenberg SJ, et al. *Multi-institutional phase I/II trial of stereotactic body radiation therapy for liver metastases.* *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* 2009; 27(10): 1572-8.

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This is not intended as a substitute for medical advice from your professional healthcare provider.  
Contact your professional healthcare provider to find out if CyberKnife is right for you.