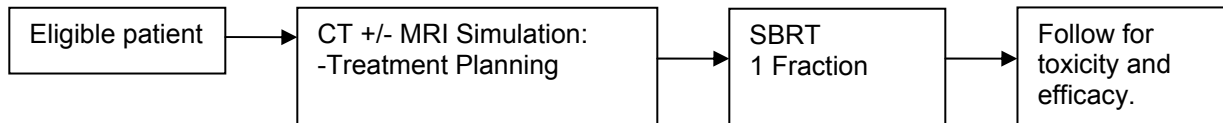


Study: Dose Escalating Study of Single Fraction Stereotactic Body Radiation Therapy (SBRT) for Patients with Hepatic Metastases

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SCHEMA



Number of patients = between 7-60 (depending on tolerance)

Patients in each dose cohort will all be treated as a single group for dose escalation. The starting dose for the dose escalation portion will be 35Gy in one fraction. Subsequent cohorts of patients will receive an additional 5Gy per treatment to a maximum planned dose of 50Gy in one fraction as follows:

<u>No. Fractions</u>	<u>Dose per fraction (Gy)</u>	<u>Total Dose (Gy)</u>	<u>No. Patients</u>
1	35	35	7-15
1	40	40	7-15
1	45	45	7-15
1	50	50	7-15

Minimum waiting periods will be assigned between each dose cohort to observe toxicity. The study will be completed when dose limiting toxicity is reached or when the maximum planned dose (50Gy) is attained to consider the therapy likely to be highly efficacious.

OBJECTIVES

- The primary objective is to escalate the dose of single fraction stereotactic radiotherapy to a tumoricidal dose without exceeding the maximum tolerated dose in patients with hepatic metastases.
- Secondary Objectives
 - To determine the dose-limiting toxicity (if the maximum tolerated dose is reached).
 - To describe the actuarial 6 and 12 month local control rates, to ascertain an optimal therapeutic window between control and toxicity, the 3 month tumor response rate, and survival for patients receiving single fraction stereotactic radiotherapy to their hepatic metastases.

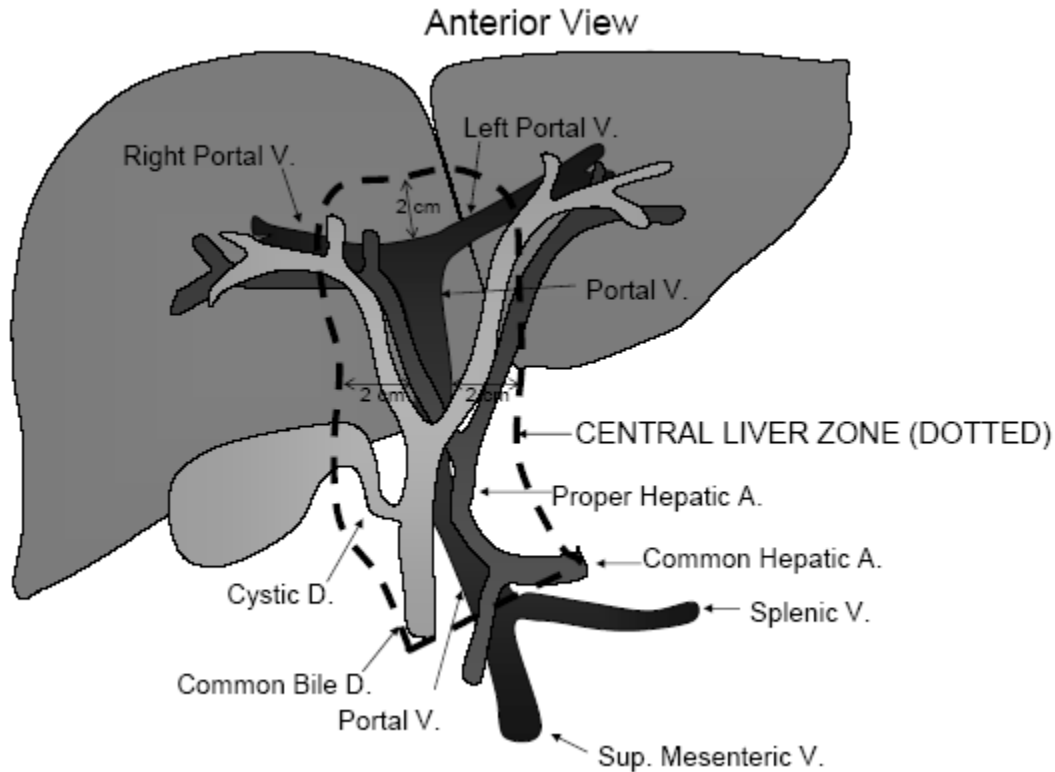
PATIENT SELECTION

Inclusion Criteria

Patients must meet all of the following inclusion criteria to be eligible for participation in this study:

1. Signed study specific informed consent form.
2. Age \geq 18.

3. Zubrod Performance Status 0-2.
4. Biopsy proven primary malignancy.
5. Predicted survival of >6 months.
6. AJCC Stage IV disease with up to 5 liver metastases as seen on a contrast-enhanced CT, MRI or PET/CT.
7. Ability to spare a critical liver volume as defined by the protocol constraints.
8. Tumors must be located outside the Central Liver Zone defined by contouring the portal vein to its bifurcation + a 3-dimensional 2cm margin (See 6.5.2.11 and diagram below).



Exclusion Criteria

Patients who meet any of the following exclusion criteria are not to be enrolled in this study:

1. Patients with a history of prior irradiation or other treatment to the liver or abdomen who after the protocol treatment would have cumulative doses to the liver or other normal tissues greater than the protocol defined constraints.
2. Need or plans for concomitant antineoplastic therapy (including surgery, cryotherapy, radiofrequency ablation, chemo-embolization, conventionally fractionated radiotherapy, brachytherapy, and hepatic artery chemotherapy) for the protocol treated lesions except at progression. Adjuvant systemic therapy before and after the protocol therapy per section 7.0, and surgery or other ablative therapy is allowed for lesions appearing after enrollment to this protocol as per section 8.0 is allowed.
3. Germ cell or hematologic malignancies.
4. History of Crohn's Disease or Ulcerative Colitis.
5. Active peptic ulcer disease.
6. Underlying hepatic cirrhosis with Child-Pugh class B or C
7. A major psychiatric illness which would limit understanding of the proposed protocol treatment and consent process

8. Men and women of reproductive potential may not participate unless they agree to use an effective contraceptive method.
9. Pregnant or lactating women.
10. Severe, active co-morbidity, defined as follows:
 - a. Unstable angina and/or congestive heart failure requiring hospitalization within the last 6 months.
 - b. Transmural myocardial infarction within the last 6 months.
 - c. Acute bacterial or fungal infection requiring intravenous antibiotics at the time of registration.
 - d. Chronic Obstructive Pulmonary Disease exacerbation or other respiratory illness requiring hospitalization or precluding study therapy at the time of registration.
 - e. Active hepatitis or clinically significant liver failure.

11. Laboratory Exclusion Criteria:

Laboratory Exclusion Criteria	
Albumin	≤3 g/dL
Alkaline Phosphatase	>1.5 X Upper limits of Normal (ULN)
ALT/AST	>1.5 X ULN
Total Bilirubin	>1.5 X ULN
PT/INR*	>1.5 X ULN
Hemoglobin	<10 g/dL
Platelets	<100,000/ μm ³
ANC	<1,000/mm ³

*An exception may be made on an individual basis by the principal investigator for an elevated PT/INR that is secondary to anticoagulation.

12. Formal evaluation by the surgical oncology group at UTSW: All patients should be fairly and prudently informed of their treatment options. To this end, all patients must be evaluated by the surgical oncology group at UTSW before SBRT treatment for discussion and consideration of other options for treatment of metastatic liver cancer including surgical resection.