

A Single Institutional Series of Stereotactic Body Radiation Therapy (SBRT) for Treatment of Liver Metastases at a Low- volume, Community-based Hospital

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Background

Treatment of Oligometastatic Liver Lesions

- Aggressive local treatment with surgical resection of oligometastatic liver lesions can result in long-term survival of up to 20% of patients (Fong 1999)
- Non-operative candidates rely on ablative approaches: radiofrequency ablation, cryotherapy, yttrium 90 microsphere therapy, or ***stereotactic body radiation therapy (SBRT)***
- ***SBRT*** is able to focus a high dose of radiation to a small planned treatment volume (PTV) while sparing the majority of liver tissue (Scorsetti 2014; Goodman 2016)

Stereotactic Body Radiation Therapy for the Treatment of Oligometastatic Liver Lesions

- Retrospective and phase I/II prospective studies have shown SBRT to be a safe and effective non-invasive option for the treatment of liver metastases

2-year Local Control (LC) ranges from 67%-100%

Published Studies	2-year local control (LC)
Goodman 2016	91%
Herfath 2001	67% (18 mo)
Lee 2009	71% (1 yr)
Mendez Romero 2016	82%
Meyer 2016	100%
Milano 2008	67%
Rule 2011	89% (50 Gy cohort)
Rusthoven 2009	92%
Scorsetti 2014	91%
Vautravers-Dewas 2011	86%

Stereotactic Body Radiation Therapy for the Treatment of Oligometastatic Liver Lesions

- Phase I/II trial by Rusthoven et al. found:
 - 2-year LC for lesions with maximum diameter ≤ 3 cm: 100%
 - 2-year LC for lesions with maximum diameter > 3 cm: 77%
 - Median progression free survival (PFS) was 6.1 months
 - 2-year overall survival (OS) was 30%
- Toxicity:
 - Grade 3 soft tissue toxicity (n=1)
 - No grade 4 or 5 toxicity reported

Most current published reports are from high-volume centers

Impact of High-volume vs Low-volume centers on Treatment Outcomes

- Improved overall survival has been suggested when patients undergo technically challenging surgery for advanced cancer at high-volume centers compared to low-volume centers (Begg 1998; Bilimoria 2008; Birkmeyer 1999 and 2002; Luctenborg 2013)
- Analogous to surgery, some have suggested advanced radiotherapy techniques performed at low-volume centers result in inferior outcomes and worse overall survival (Wuthrick 2015; Hillner 2000; Lin 2014; Zumsteg 2017)

Does this hold true for the use of SBRT in the treatment of oligometastatic liver disease?

Aims of this Study

Assess the implementation of SBRT for the treatment of liver metastases at a **low-volume, community-based hospital**

via

analysis of the **efficacy and toxicity of 41 consecutively treated patients over a 10 year period** through the use of retrospective, database analysis

Methods

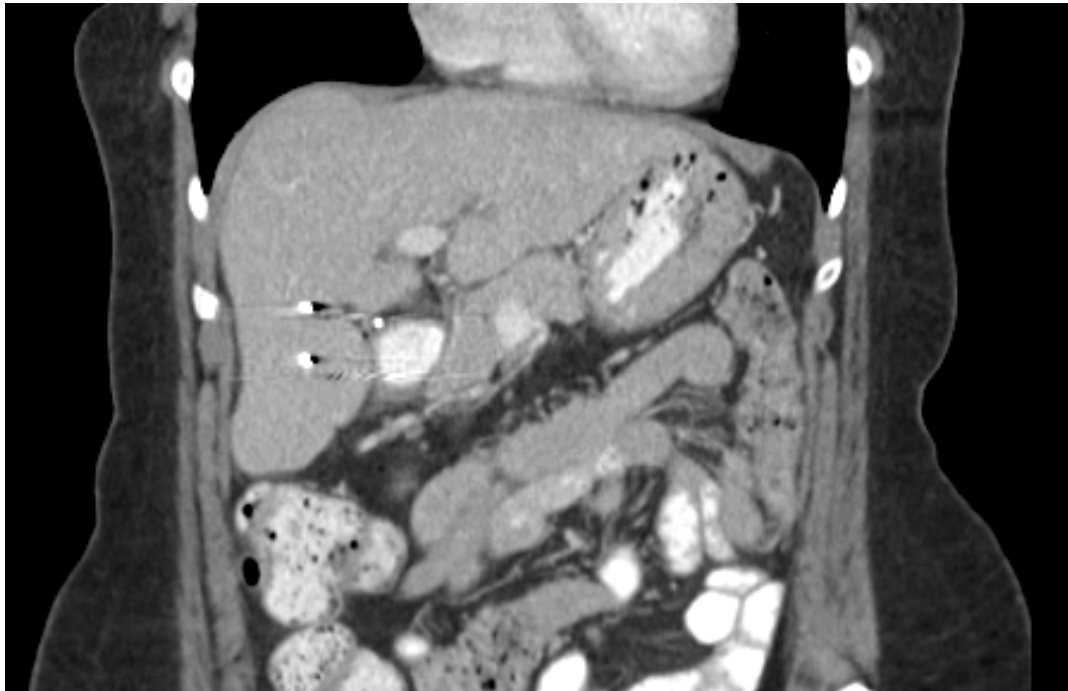
Study population

- Subjects entered into an **institutional review board approved registry** at a **community-based hospital**
- Written informed consent was obtained from patients undergoing SBRT for liver metastases from various primary tumor sites **between 2006 and 2016**
- Patients with **primary liver neoplasms were excluded** from analysis
- All eligible patients had **primary tumor controlled** at the time of treatment

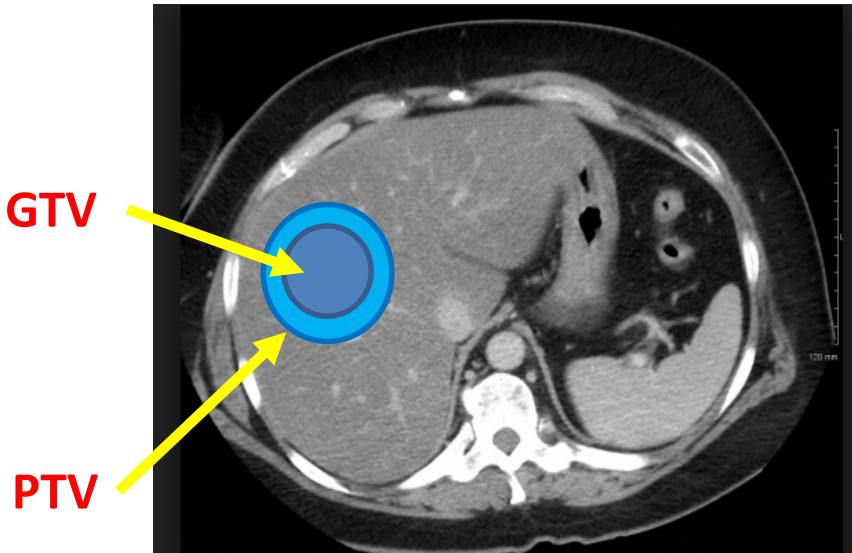
Treatments

- All patients underwent **fiducial marker placement** under CT-guidance 1-2 weeks prior to planning scans
- Gross tumor volume (GTV) was delineated using contrast enhanced CT scans, as well as fusion with positron emission tomography (PET) and/or magnetic resonance imaging (MRI) scans
- GTV was **expanded by 5 mm to create the PTV**
- Treatment was delivered by **image guided SBRT with respiratory motion tracking CyberKnife[®]**
- Lesions were treated with **3 consecutive fractions to a median total dose of 54 Gy**

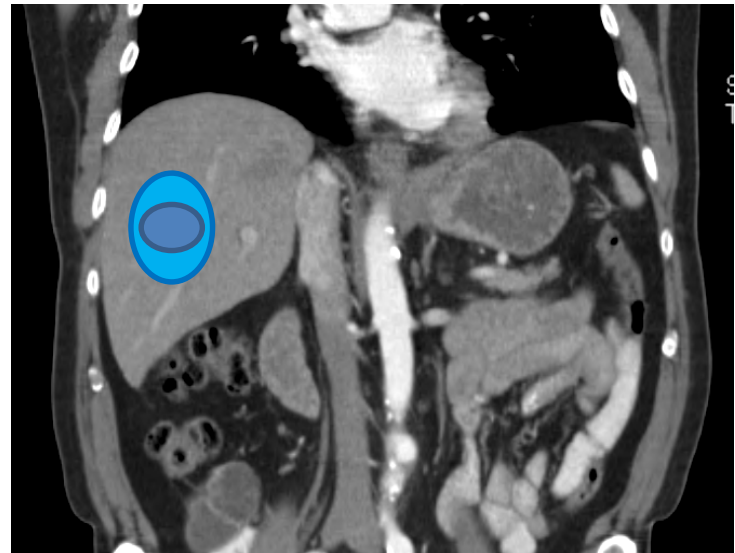
Fiducial Marker Placement



SBRT Parameters

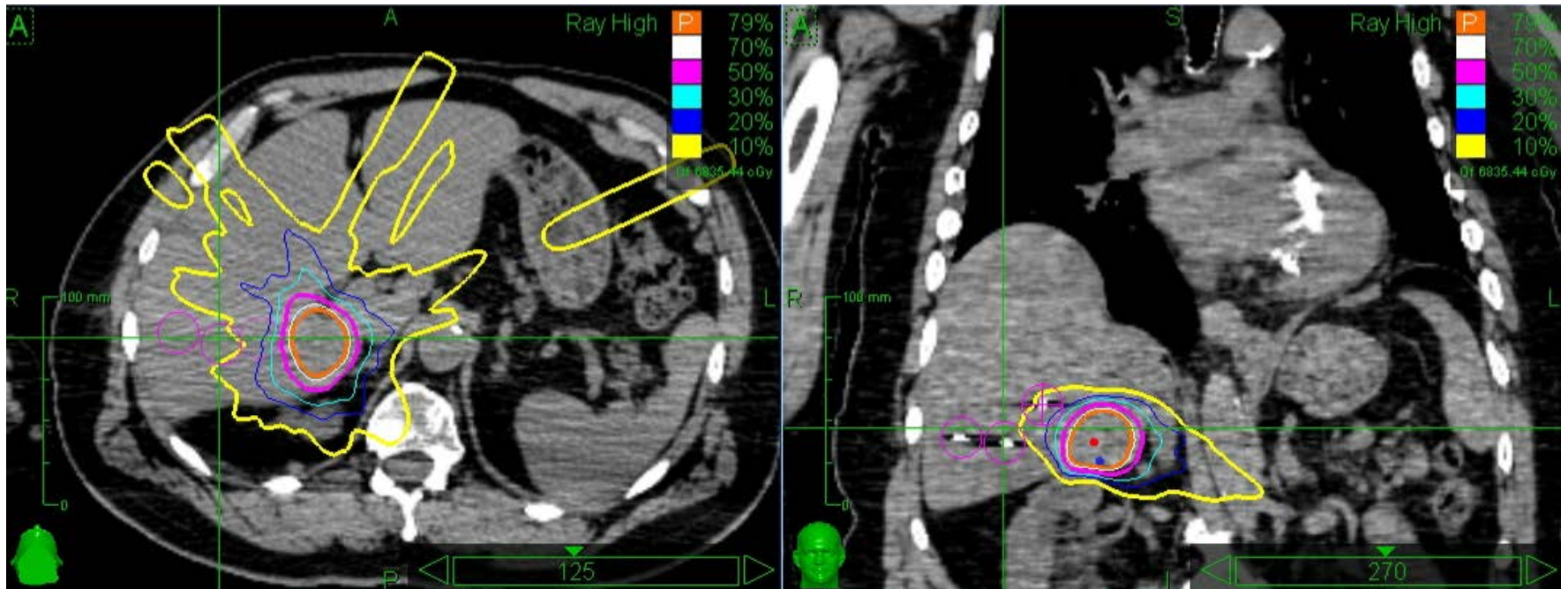


5mm radial expansion



5mm craniocaudal expansion

CyberKnife[®] Plan



PET-CT Registration



Data Collection

- Data from each patient was collected and entered into the patient registry database
- Radiation toxicities were graded according to the **Radiation Therapy and Oncology Group (RTOG) common toxicity criteria**

Statistical Analysis

- All outcomes were **defined as the time from the date of delivery of the first fraction of treatment** to death (OS), progression of disease at any site (PFS), or local progression of the treated liver lesion (LC)
- Overall survival, progression-free survival and local failure-free survival were estimated using **Kaplan-Meier method**
- **Log-rank statistic** was used to compare local control based on gross tumor volume

Results

Patient Characteristics

Characteristic	Number (% total)	Median [range]
Total patients	42	
Total lesions evaluated	81	
Age at treatment of each lesion (years)		65 [39-87]
Gender		
Male	21 (50%)	
Female	21 (50%)	
Primary tumor location		
anal	1 (2.4%)	
bladder	1 (2.4%)	
breast	3 (7.1%)	
cervical	1 (2.4%)	
colon	18 (42.9%)	
lung	7 (16.7%)	
pancreas	2 (5%)	
peritoneal	1 (2.4%)	
prostate	1 (2.4%)	
rectal	1 (2.4%)	
renal	2 (5%)	
stomach	1 (2.4%)	
uterine	3 (7.1%)	
Presence of extrahepatic disease at treatment of each lesion		
Yes	12 (15.6%)	
No	65 (84.4%)	
Time since primary diagnosis (months)		26 [6-216]
Karnofsky performance score		90 [70-100]

Lesion & Treatment Characteristics

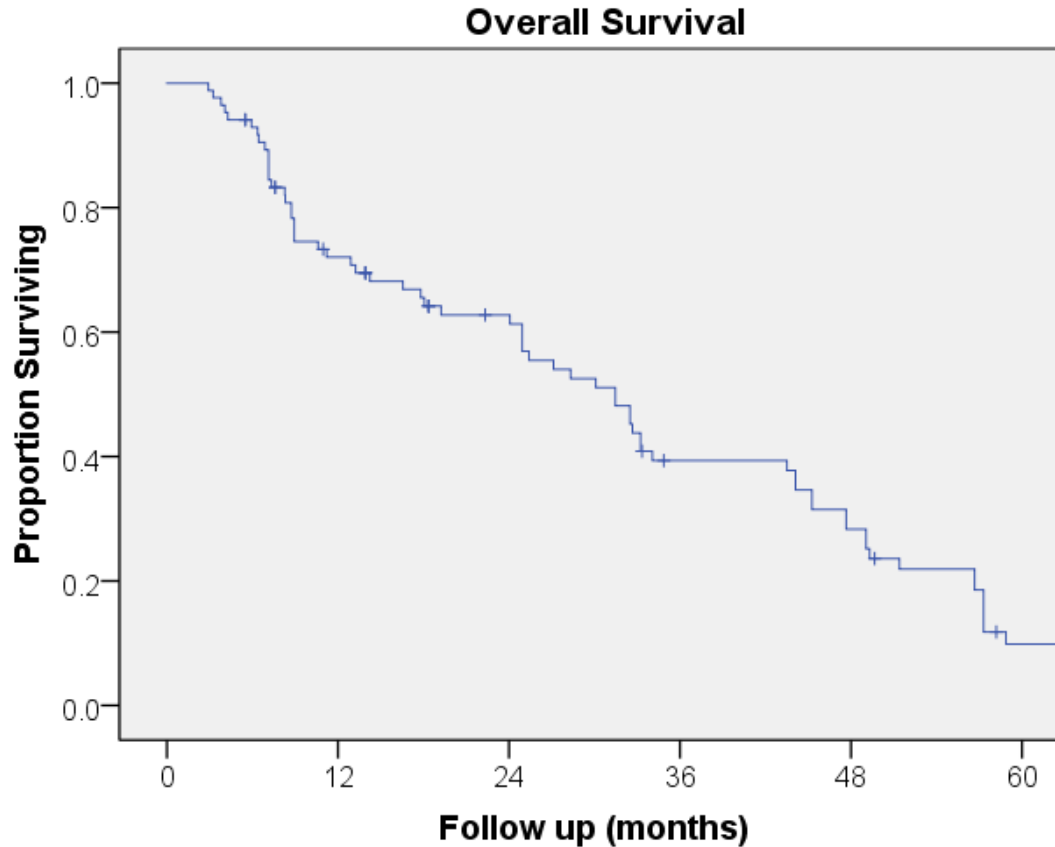
Characteristic	Number (% total)	Median [range]
Prior local therapy		
SBRT	16 (20%)	
Resection	2 (2.5%)	
Cryoablation	1 (1.2%)	
Multiple	8 (9.9%)	
None	54 (66.7%)	
Liver lesions treated at one time		1 [1-4]
Liver lesions treated per patient		1 [1-6]
Max diameter of each lesion		2.5 cm [0.5-9.5 cm]
Fraction and Dosage		3 x 18 Gy [14-20 Gy]
Isodose line		78 % [56-86%]

Outcomes

Parameter	Number (% total)	Median [range]
Months of Follow-up		24.9 mo [2.9-100.9]
New liver mets	27 (33.3%)	
Time to new liver mets		6 mo [1-52]
New extrahepatic mets	12 (15.6%)	
Total treatments	57	
Max local response		
Stable	7 (8.6%)	
PR	17 (21.0%)	
CR	45 (55.6%)	

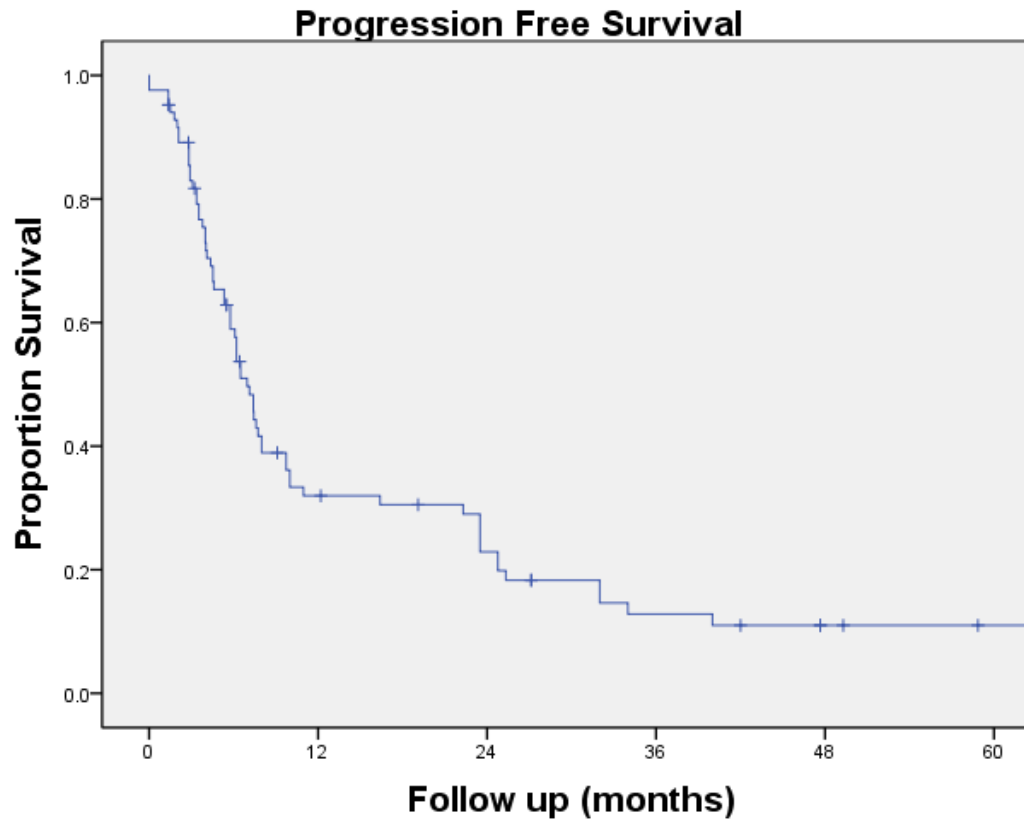
Overall Survival

Parameter	Number (% total)	Number (% total)
	<i>1 year</i>	<i>2 years</i>
Overall Survival	72.0%	62.0%



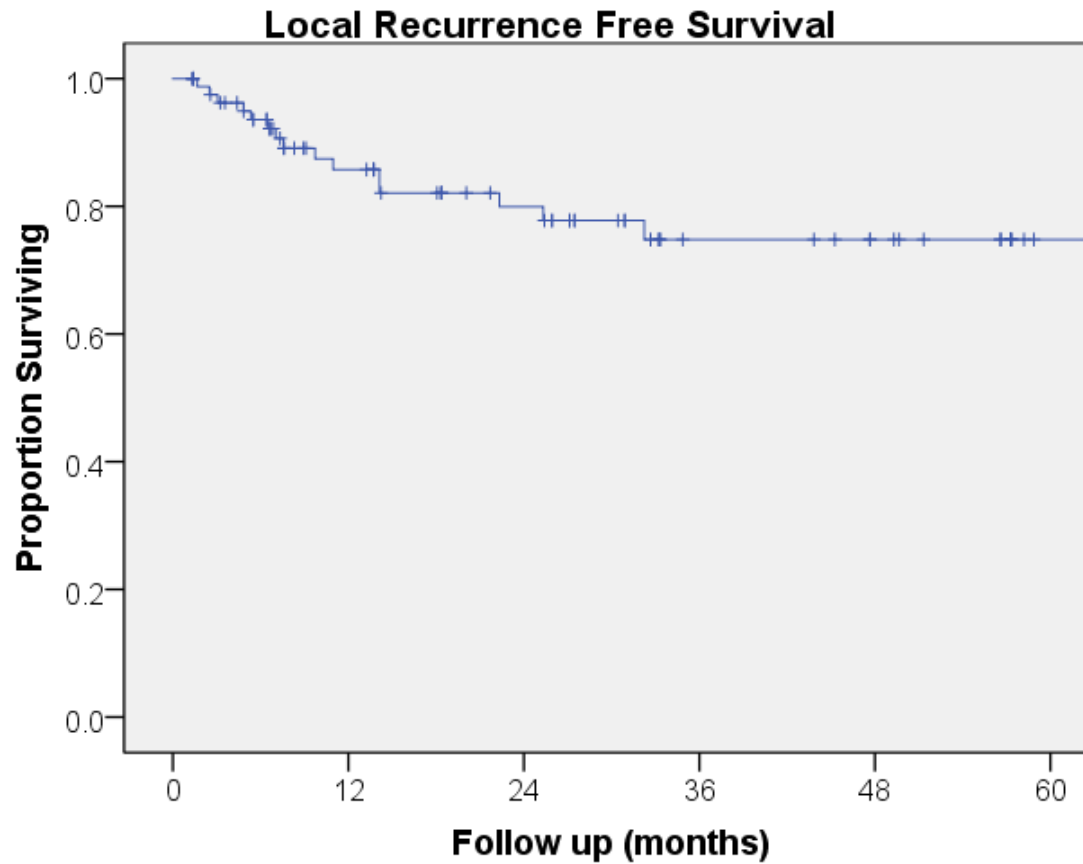
Progression Free Survival

Parameter	Number (% total)	Number (% total)
	<i>1 year</i>	<i>2 years</i>
Progression Free Survival	32.0%	23.0%



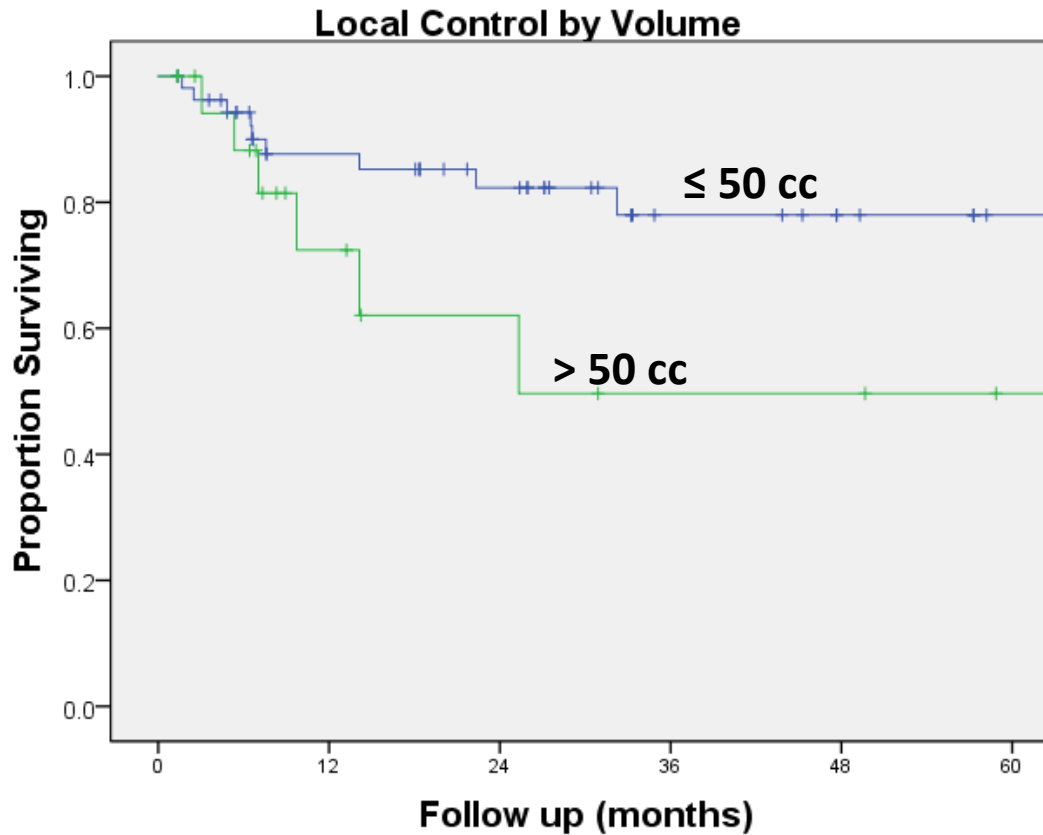
Local Control

Parameter	Number (% total)	Number (% total)
	1 year	2 years
Local Control	86.0%	80.0%



Local Control by Volume

Parameter	Number (% total)
	<i>2 years</i>
Local Control	
≤ 50 cc	87.5%
> 50 cc	70.0%



Toxicities

Parameter	Number (% total)	Median [range]
Toxicity grade and type		0 [0-2]
0	41 (71.9%)	
1	12 (21.1%)	Fatigue (4), Diarrhea (1), Skin irritation (2) , Nausea (4), Pneumonitis (1)
2	3 (5.3%)	Chest wall pain (1), Nausea/Vomiting/RUQ pain/Rib fracture/elevated LFTs (2- same person, two rounds of treatment)

Conclusions

- This 10-year patient registry database has allowed for **analysis of the efficacy and safety of SBRT for liver metastases at a low-volume, community-based hospital for the first time**
- The **results found are comparable** to available published data at high-volume institutions regarding the efficacy and toxicity of this technology:
 - Current published studies from high-volume institutions on SBRT for liver metastases show LC at 2 years ranges from 67% to 100%, while **in this analysis LC at 2 years was found to be 80%**
 - We found that **toxicities associated with SBRT for liver metastases did not exceed grade 2**, while previously published studies showed examples of grade 3-5 toxicities

Discussion

- **Strengths of this study:**
 - Consistency of the treatment parameters each patient received
 - Exclusively metastatic lesions and not primary liver cancer
 - Long follow-up time achieved for many of the patients
- **Limitation of this study:**
 - Modest patient population at a single institution
- **Future direction:**
 - Larger-scale, multi-institutional study at low-volume institutions powered to compare outcomes to high-volume centers

Summary

These findings demonstrate successful, safe implementation of a liver metastasis SBRT CyberKnife® program at a low-volume, community hospital center and suggest this technology should not be limited to high volume centers

Thank You!