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Proton SBRT/Hypofractionation for Liver

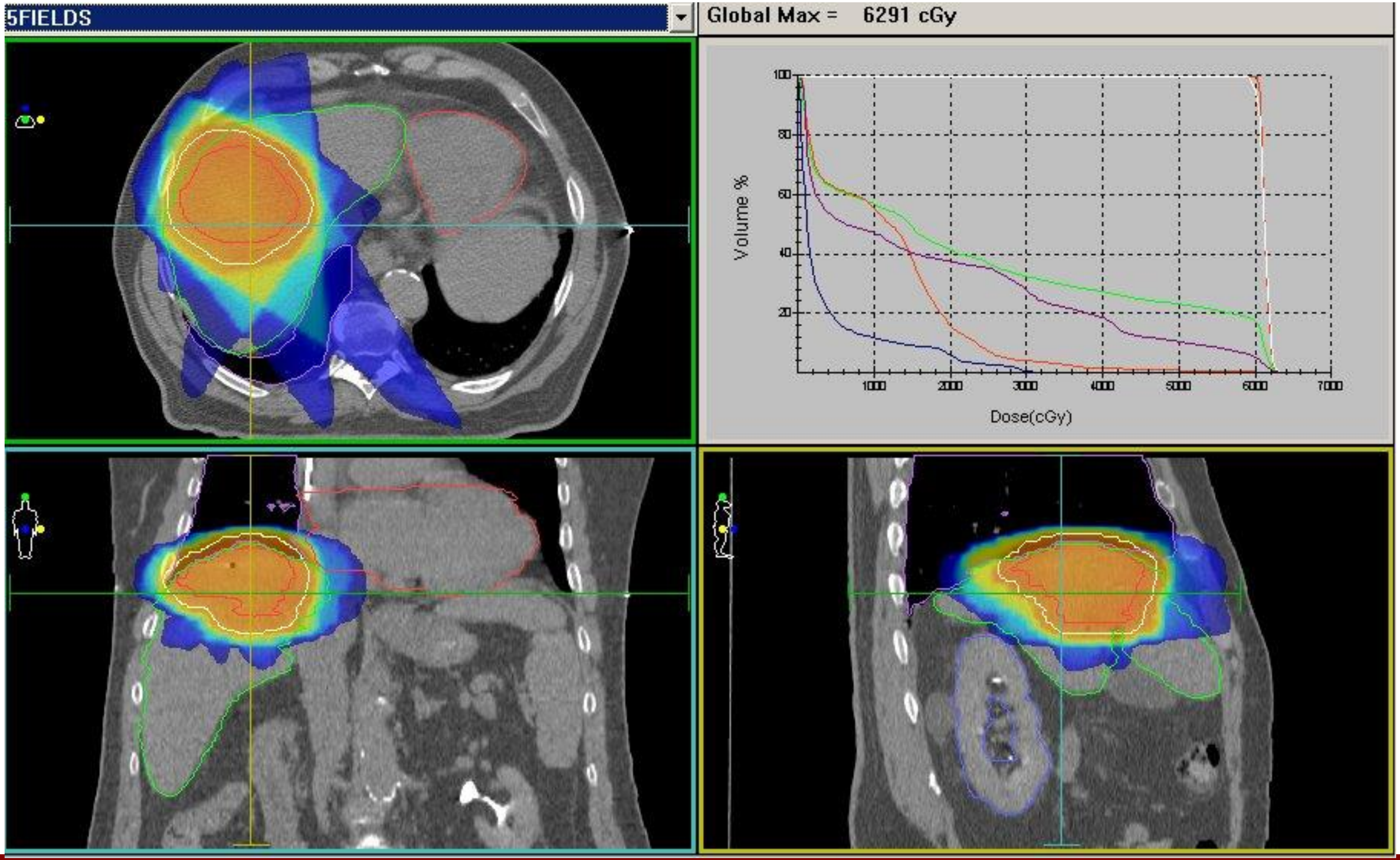
Theodore S. Hong, MD
Director, Gastrointestinal Radiation Oncology
Massachusetts General Hospital
Senior Clinical Investigator
MGB Data Science Office
Professor of Radiation Oncology
Harvard Medical School

Liver Survey Overview

- Survey designed by NRG Proton SBRT Working Group
- Sent to all US proton centers participating in NRG trials in Summer 2021
- 66 survey questions, covering 5 categories
  - Vendors, Delivery Techniques, and TPS (1-4)
  - Patient Selection (5-13)
  - Simulation and Motion Management (14-19)
  - Treatment Planning and QA (20-52)
  - Motion and IGRT (53-66)

- Focus today: questions that received wide variety of responses

SBRT PLAN



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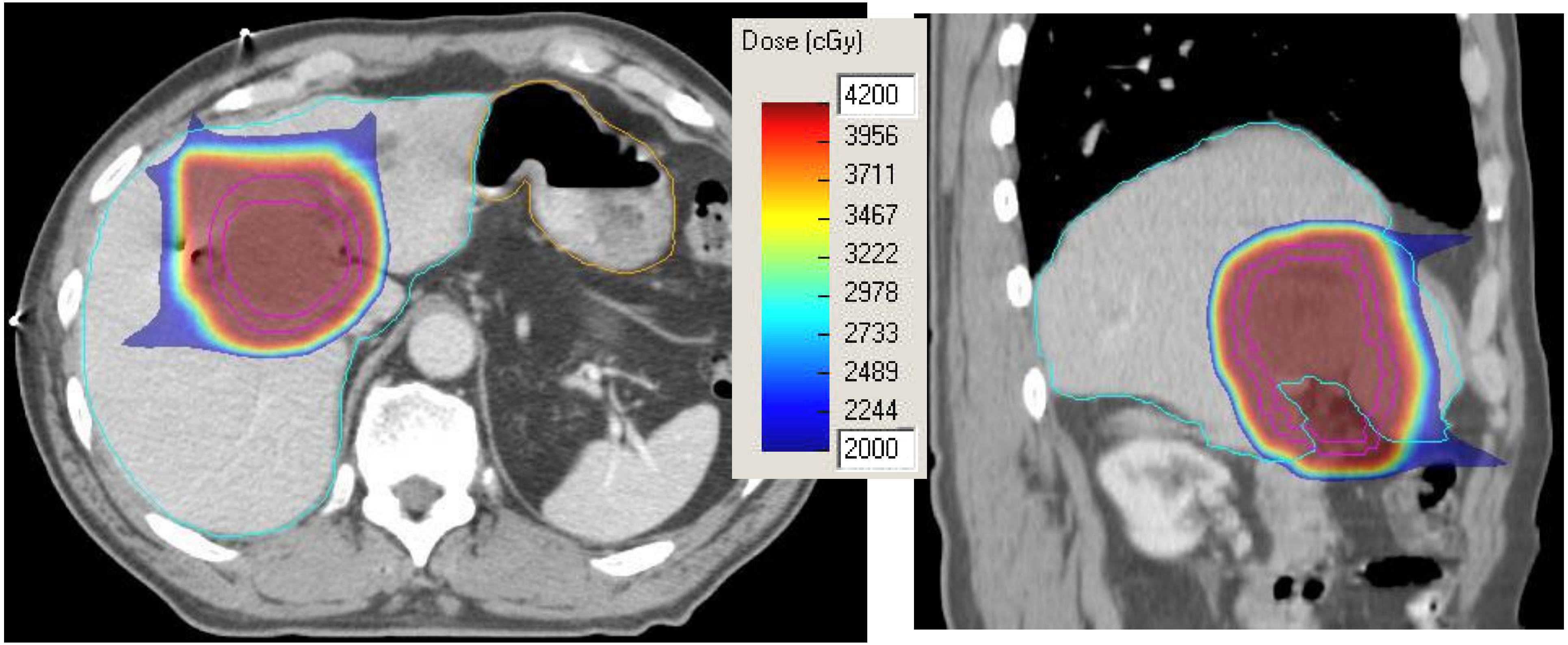


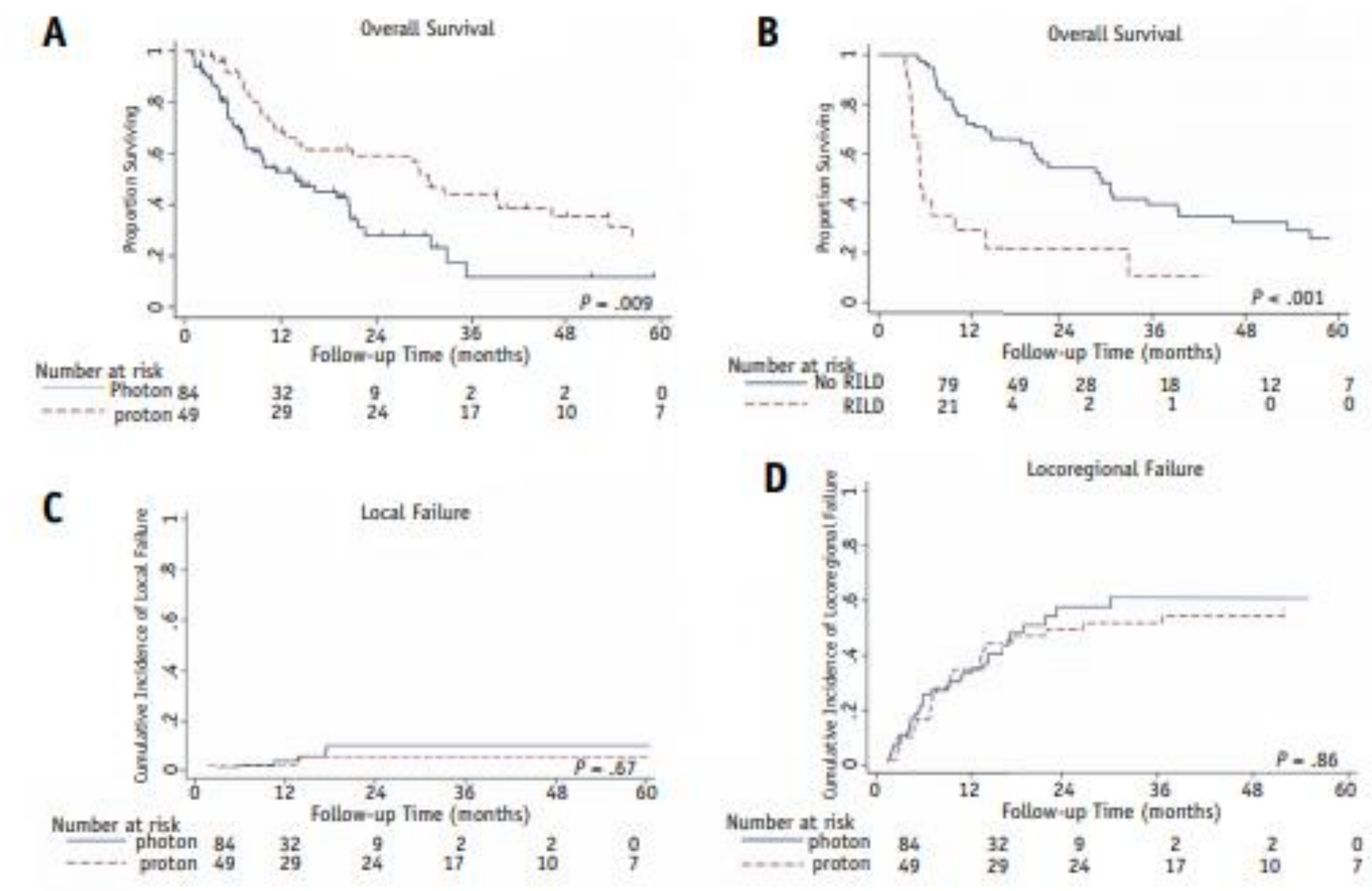
Is Survival for HCC after Radiation Driven by LC or Toxicity?

Number of Patients	102	92
Number of Fractions	6 fractions	15 fractions
Median Dose	36 Gy	58.05 Gy
BED Dose	57.6	80.4
Local Control*	87% (1 year)	95% (2 year)
Worsening of CP Score at 3 Months	29%	3%
2-Year Overall Survival	40%	71%

[1]Bujold et al. JCO, 31(13):1631-9, 2013.
[2]Hong TS, et al. JCO, 34(5): 460-8, 2016.

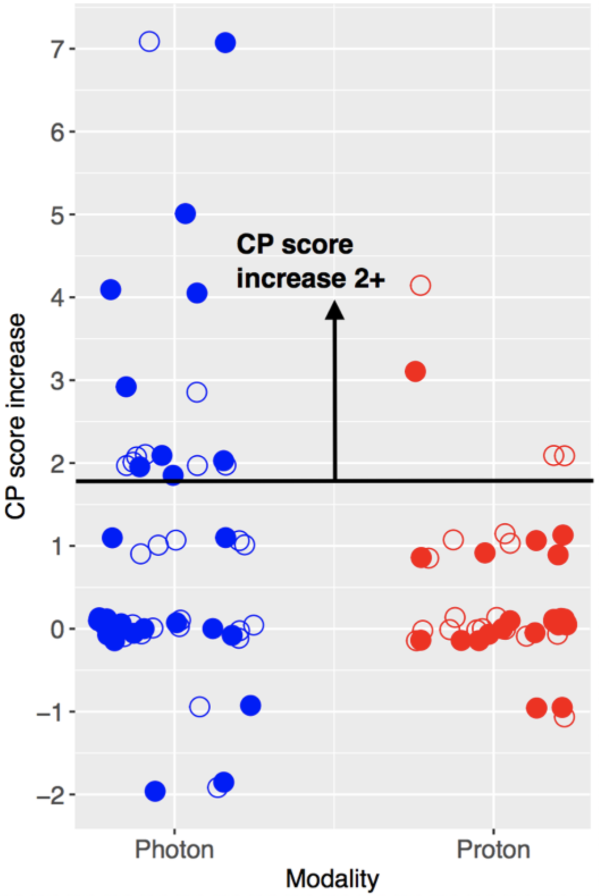
MGH Series: Protons Better than Photons?

- N=133 patients treated at MGH (84 pts with photons, 49 pts with protons)
- Results:
  - No difference in LF (LF: 6% vs. 8%, p=NS)
  - Improved OS with protons (median OS: 31 mo vs. 14 mo, p=0.009)



Sanford NN, et al. IJROBP 105(1): 64-72; 2019.

MGH Protons vs Photons: CP increase based on modality, liver dose



•Improved OS likely secondary to less liver decompsensation post RT

Solid: Mean liver-GTV dose > 21.6 Gy

Empty: Mean liver-GTV dose < 21.6 Gy

Sanford NN, et al. IJROBP 105(1): 64-72; 2019.

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Is Survival for HCC after Radiation Driven by LC or Toxicity? Multivariable Analysis

Table 2: Multivariable Analysis for Overall Survival and Locoregional Failure						
	OS			LF/LRF		
Variable	HR	95%CI	P-value	HR	95% CI	P-value
Proton	0.48	0.28-0.83	0.009	0.97	0.56-1.70	0.93
ECOG (2/3 vs. 0/1)	2.29	1.53-3.43	<0.001	0.59	0.35-0.99	0.05
Child-Pugh (B/C vs. A)	1.88	1.05-3.31	0.03	0.60	0.26-1.38	0.23
Thrombus (yes vs. no)	2.06	1.20-3.53	0.008	0.87	0.47-1.61	0.65
GTV (> vs. ≤ median)	1.59	0.93-2.74	0.09	2.04	1.11-3.74	0.02
Tumor dose (> vs. ≤ median)	0.56	0.33-0.96	0.04	0.80	0.45-1.43	0.46
Mean liver dose (> vs. ≤ median)	1.29	0.74-2.27	0.37	1.08	0.59-1.96	0.81

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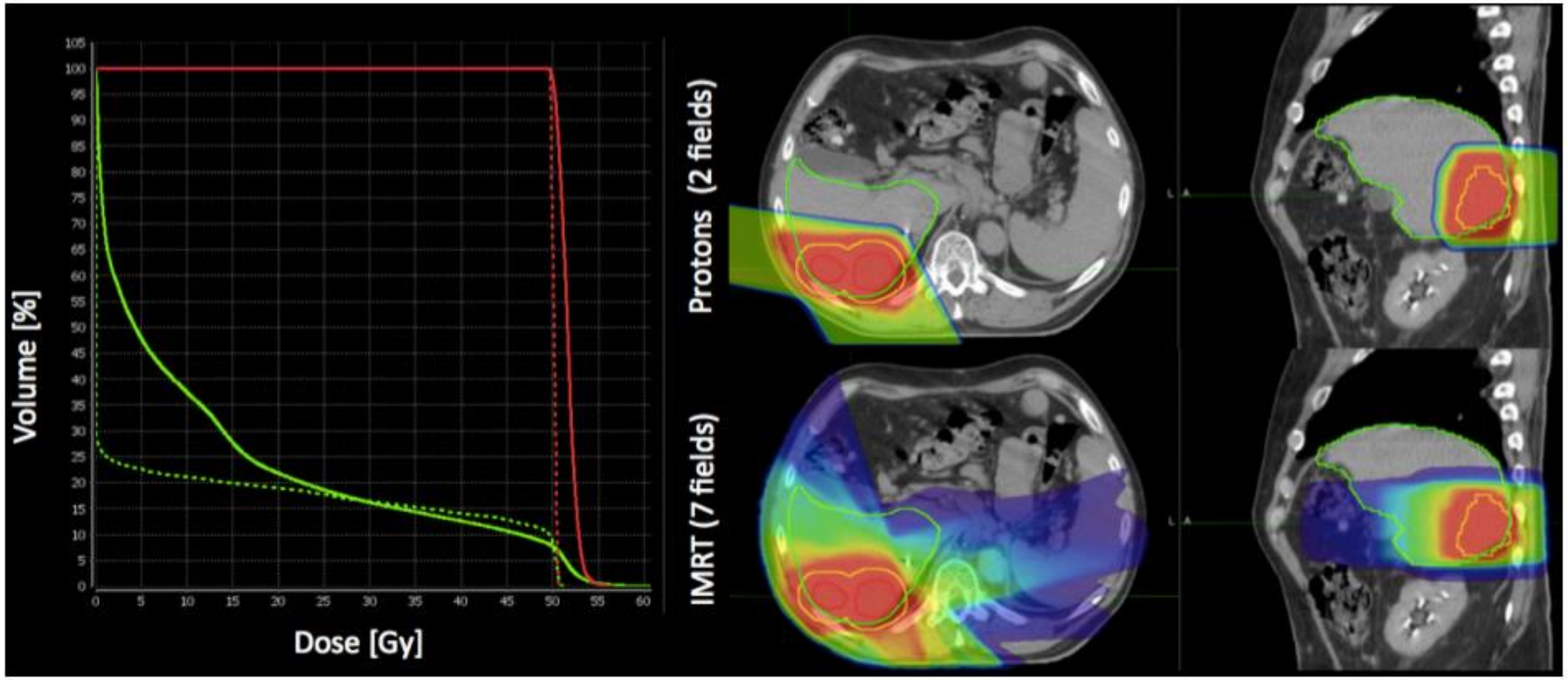
Dosimetric Analysis

	Photons	Protons	
Mean liver dose, Gy, Median (IQR)	22 (19-25)	22 (17-28)	0.97
Dose delivered, Gy, Median (IQR)	67 (67-82)	67 (60-70)	0.20
rV10Gy, Median (IQR)	50.5 (43.8-59.9)	60.0 (51.5-71.0)	0.0003



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Response Overview

- Response Rate: 66%
- 18 centers treat liver SBRT and/or Hypofractionation with protons
- 1 center will implement in the near future (Beaumont)

Institution	Liver Q
Penn	x
MDA	x
MGH	x
UFPTI	
OKC	
Northwestern	x
LLUMC	x
NJ Procure	x
Hampton	
SCCA	x
Wash U	x
CA Protons	
Provision	x
Willis Knighton	x
RWJ	x
TX CPT	
Maryland	
Mayo Rochester	
Mayo AZ	x
UF Orlando	x
CASE	
Cincinnati	
Beaumont	x
Miami Cancer Inst	
Emory	x
NYPC	x
UOHSC	x
Johns Hopkins	x
Inova Schar	x

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Barriers to Using Protons for Liver Cancer

- Motion
  - MGH started as passively scattered, which is somewhat more motion insensitive
  - Move to pencil beam has limited our organ motion to 5 mm peak to peak which severe limits cases based on internal robustness analysis- requires re-scanning
  - Gating more complex
- Conformality
  - Sometimes for tumors abutting mucosal surfaces, photons may have better conformality

Vendors, Delivery Techniques, and TPSs

Vendors			Techniques			TPS		
IBA	9	47%	PBS	14	70%	Raystation	11	58%
Mevion	4	21%	Passive Scatter	5	25%	Eclipse	6	32%
ProBeam	2	11%	Uniform scanning	1	5%	others	2	11%
Hitach	3	16%	tot	20		tot	19	
Optivus	1	5%						
tot	19							

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Questions for Physician Discussion

- Prescription for liver SBRT (rationale, dose uniformity or dose heterogeneity consideration…)
- Protocols for target delineation (internal, NRG, or others)
- The future improvement for proton liver SBRT (planning, motion, IGRT…)

Discussion Point: Patient Selection

Survey Question	Answers	# Responses	% Responses
Both primary and metastases	Technically/medically inoperable	17	94%
	No answer	1	6%
How many lesions are treated?	less 3	18	100%
What is the maximum tumor diameter allowed?	No limit	12	67%
	GI003 12cm	2	11%
	5cm	1	6%
	15cm	1	6%
	No answer or other	2	11%
How much uninvolved liver is acceptable?	700cc	16	89%
Do you perform SBRT/hypofraction reirradiation?	Yes	13	72%
	No	4	22%
	No answer	1	6%

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Discussion Point: Prescriptions

Survey Question	Total dose/# fx	# Responses	% Responses
Rx for primary liver cancers?	45 Gy / 5 fx	3	11%
	50 Gy / 5 fx	11	39%
	60 Gy / 3 fx	1	4%
	67.5 Gy / 15 fx	3	11%
	70.2 Gy / 15 fx	1	4%
Rx for metastases?	70 Gy / 10 fx	1	4%
	75 Gy / 25 fx	1	4%
	63 Gy / 15 fx	1	4%
	GI003 for diff dose level	1	4%
	30 Gy / 5 fx	2	7%
	Depends on histology, size, DVH, etc.	1	4%
	45-67.5 Gy / 15 fx	1	4%
	NTCP based model	1	4%

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Discussion Point: Planning Volumes & Margins

What is the main target for planning?	CTV/ITV	14	86%
	PTV	4	29%
Do you use a uniform margin from GTV to CTV?	Yes	11	79%
	No	6	43%
	Sometimes	1	6%
If a uniform margin is used, what is the margin?	3 mm	1	6%
	5 mm	7	39%
	Others	10	56%
If a uniform margin is used, do you crop out normal structures?	Yes	10	56%
	No	5	28%
	No specification	3	17%
If you crop out normal structures, which OARs do you crop? (e.g. duodenum, stomach, etc.)	Yes (duodenum, lung, ribs, stomach, bowel, chest wall)	10	56%
	No/did not specify	8	57%

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Discussion Point: What technology would make you more likely to treat liver with proton SBRT?

- Treatment planning capabilities?
- Motion management capabilities?
- IGRT technology?