



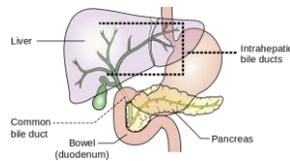
Clinical Aspects of SBRT in Abdominal Regions

Brian D. Kavanagh, MD, MPH
University of Colorado
Department of Radiation Oncology



Abdominal SBRT: Clinical Aspects

- Rationales for liver and pancreas SBRT
- Dose-tumor control reports
- SBRT v other modalities



Rationales for liver SBRT

- For liver metastases
 - to try to extend disease-free and overall survival for patients with oligometastatic disease
- For primary hepatocellular carcinoma (HCC)
 - potentially curative therapy in medically inoperable cases
 - maybe an alternative to surgery ?
 - as a "bridge" to transplant for selected cases in centers with expertise in this area

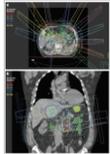
What is currently the best evidence for these indications?

- **Liver SBRT for metastases**
 - various encouraging phase II studies
 - randomized data for one stage IV tumor type (lung cancer) showing improved PFS with consolidative RT in the oligometastatic setting
- Liver SBRT for primary HCC
 - various encouraging comparative effectiveness studies
- Pancreas SBRT
 - encouraging recent prospective phase II data

Radical Irradiation of Extracranial Oligometastases

Joseph K. Salama and Michael T. Milano

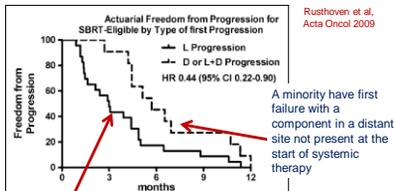
J Clin Oncol 32:2902-2912. © 2014



Study	Year	Design	Arm	n	Median PFS (mo)	HR (95% CI)	OS (mo)	Local Control (%)
Salama et al	2013	Phase II	SBRT	15	12.1	0.44 (0.22-0.90)	12.1	100
Milano et al	2013	Phase II	SBRT	15	12.1	0.44 (0.22-0.90)	12.1	100
...

Study	Year	Design	Arm	n	Median PFS (mo)	HR (95% CI)	OS (mo)	Local Control (%)
...

Oligometastatic lung cancer: Patterns of Failure in metastatic NSCLC



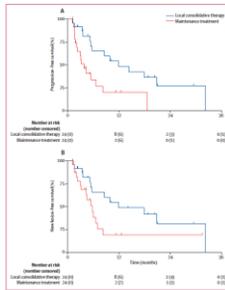
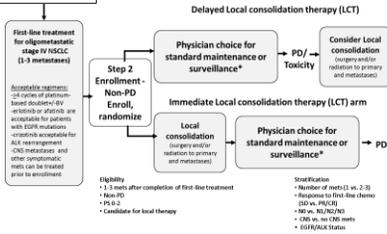
Rusthoven et al, Acta Oncol 2009

A minority have first failure with a component in a distant site not present at the start of systemic therapy

After 1st line systemic therapy, 2/3 of patients have first failure in initially involved sites, with median PFS of 3 mos

Local consolidative therapy versus maintenance therapy or observation for patients with oligometastatic non-small-cell lung cancer without progression after first-line systemic therapy: a multicentre, randomised, controlled, phase 2 study

The Lancet Oncology 17, no. 12 (2016): 1672-1682.



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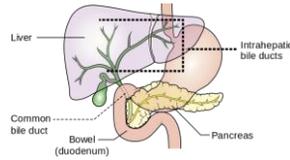
therapy group compared with the maintenance treatment group. Specifically, the Data Safety Monitoring Committee found that based on the current data, the probability of concluding in favour of the local consolidative therapy group was 99.46% if the current trend were to continue. Therefore, upon the recommendation of the Data Safety Monitoring Committee, the principal investigators decided to close the study to new patient entry. Data were

comments on the Gomez study

- only a few liver metastasis patients in that particular trial
- at least 6 or more similarly constructed studies of systemic therapy (chemo or molecular) with v without some form of consolidative local therapy
 - but note negative results reported at ASCO this year for combined prospective randomized studies of first-line selective internal radiotherapy (SIRT) in patients with liver metastases from colorectal cancer.
- countless studies of radiotherapy + immunotherapy, some randomized as immuno +/- RT
 - which makes me nervous....

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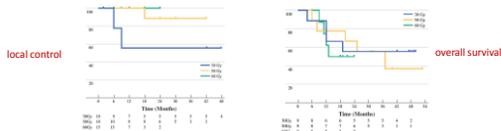


under review with TPC and Science Council:
HyTEC Liver TCP paper

HyTEC: Organ-Specific Paper	Abdominal: Liver TCP
Local Control following Stereotactic Body Radiation Therapy for Liver Tumors	
Nitin Ohri, M.D. ¹ , Andrew Jackson, Ph.D. ² , Alejandra Méndez Romero M.D. ³ , Moyed Miffen, Ph.D. ⁴ , Randall K. Ten Haken, Ph.D. ⁵ , Laura A. Dawson, M.D. ⁶ , Jimm Grimm, Ph.D. ⁷ , Ellen Yorke, Ph.D. ² , Wolfgang A. Tomé, Ph.D. ¹	

<p>Annals of SURGICAL ONCOLOGY OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGISTS</p> <p>Phase I Dose-Escalation Study of Stereotactic Body Radiotherapy in Patients With Hepatic Metastases</p> <p>William Rabe, MD¹, Robert Timmerman, MD², Lijun Tang, MS³, Raneei Abdulrahman, MD⁴, Jeffrey Meyer, MD⁵, Thomas Soko, MD⁶, Barbara E. Schwartz, MD⁷, Paul Wozniak, MD, PhD⁸, and L. Chasen Cho, MD⁹</p>	<p>Prior liver-directed therapy</p> <table border="1"> <tr><td>RFA</td><td>4 (14.8%)</td></tr> <tr><td>Resection</td><td>4 (14.8%)</td></tr> <tr><td>Resection + RFA</td><td>2 (7.4%)</td></tr> <tr><td>Chemembolization</td><td>1 (3.7%)</td></tr> <tr><td>Alcohol Ablation</td><td>1 (3.7%)</td></tr> <tr><td>Prior systemic therapy</td><td>22 (81.5%)</td></tr> </table>	RFA	4 (14.8%)	Resection	4 (14.8%)	Resection + RFA	2 (7.4%)	Chemembolization	1 (3.7%)	Alcohol Ablation	1 (3.7%)	Prior systemic therapy	22 (81.5%)
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Chemembolization	1 (3.7%)												
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Prior systemic therapy	22 (81.5%)												

10 Gy x 3, 10 Gy x 5, 12 Gy x 5
SFED 26.4, 52.8, 56.4 Gy



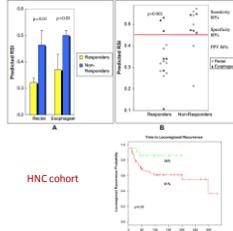
Ann Surg Oncol (2011) 18:1081–1087

Candidate Biological marker of SBRT response

BIOLOGY CONTRIBUTION
A GENE EXPRESSION MODEL OF INTRINSIC TUMOR RADIOSENSITIVITY: PREDICTION OF RESPONSE AND PROGNOSIS AFTER CRYSTALLIZATION
 Simon A. Eckardt, Ph.D.,¹ Jason Proulx, M.D.,¹ Spencer Deane, Ph.D.,² Robert East, B.S.,² David Brackner, M.D.,² Zhonghua Liu, D.D., Ph.D.,² Gregory Brown, Ph.D.,² Chad Rittenbach, M.D.,² Scott Roberts, M.D.,² Patricia P. Caron, M.D.,² Thomas P. Pridmore, M.D.,² Andrew C. Brant, Ph.D.,² and Jayesh P. Tomita-Rice, M.D.,²

- 10 "hub" genes analyzed
- SF 2Gy results across 48 cell lines used to generate model

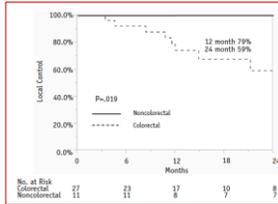
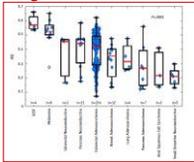
$$RSI = -0.009809 \cdot AR + 0.0128263 \cdot ckit + 0.0254352 \cdot STAT1 - 0.0017599 \cdot PKC - 0.0031171 \cdot BclA + 0.1070213 \cdot cAbl - 0.0002909 \cdot SLC10A1 - 0.0002033 \cdot CTSL - 0.0204949 \cdot HES1C - 0.0041083 \cdot RPL1$$



Int. J. Radiation Oncology Biol. Phys., Vol. 75, No. 2, pp. 489-496, 2009

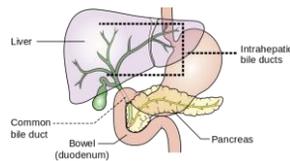
Ahmed et al, IJROBP 95(5), 1399-1404, 2016

- RSI determined from previously resected liver metastases
- Prediction of outcomes after SBRT generated



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A randomized phase II study of individualized stereotactic body radiation therapy (SBRT) versus transarterial chemoembolization (TACE) as a bridge to transplant in hepatocellular carcinoma (HCC). Nugent et al, ASCO 2017

- Pts with C-P < 9 and HCC within Milan Criteria were randomized between two arms
- TACE pts received 2 treatments one month apart using DEBDOX beads
- SBRT = 45 Gy /5 fractions.
- preliminary results shown

	SBRT = 13	TACE = 17
Age	63.3	60.6
% Stage I	85%	88%
C-P Score	5.7	5.8
Median Follow Up	237 Days	154 Days
Toxicity Events (G2-4)	23%	65%
Reduction in QOL	-0.65 (+/- 7.4)	-2.65 (+/- 4.4)
% Recurrence	0%	24%
Residual Dz on Explantz/6		4/7

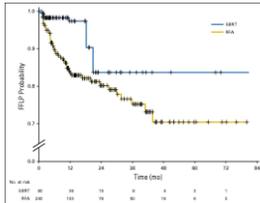
Outcomes After Stereotactic Body Radiotherapy or Radiofrequency Ablation for Hepatocellular Carcinoma.

Wahl et al, JCO. 2015 Nov 30;34(5):452-9.

Table 3. Multivariate Cox Proportional Hazards Analysis of Factors Associated With Local Progression

	HR	95% CI	P
Treatment			
RFA v SBRT	3.84	1.62 to 9.09	.002
Age	1.01	0.97 to 1.06	.514
Tumor size	1.35	0.99 to 1.84	.055
Child-Pugh score	0.95	0.74 to 1.22	.703
AFP	1.12	0.97 to 1.30	.136
No. prior treatments	1.25	1.00 to 1.56	.055

NOTE: Age (per year), tumor size (per cm), Child-Pugh score (per point), AFP (per doubling) and No. prior treatments (per treatment) were treated as continuous variables.
Abbreviations: AFP, alpha-fetoprotein; HR, hazard ratio; RFA, radiofrequency ablation; SBRT, stereotactic body radiation therapy.



Clinical Investigation

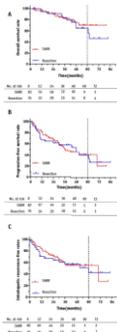
Long-Term Survival Analysis of Stereotactic Ablative Radiotherapy Versus Liver Resection for Small Hepatocellular Carcinoma

Ting-Shi Su, MD,^{1,2} Ping Liang, MD,^{1,2} Jian Liang, PhD,¹ Huan-Zhen Lu, BS,¹ Hua-Yan Jiang, BS,¹ Tao Cheng, BS,¹ Yong Huang, MD,¹ Yang Tang, BS,¹ and Xin Deng, PhD¹

¹Department of Radiation Oncology, CyberKnife Center, and ²Department of Medical Oncology, Rui Kang Hospital, Guangxi Traditional Chinese Medical University, Nanning, Guangxi Zhuang Autonomous Region, China

UROBP online Mar 1, 2017

117 pts: 82 SBRT, 35 Surgery
tumors 1.1-5cm diameter
SBRT: 42-48 Gy/3-5 fractions





Thanks for your attention!
