NCCN Guidelines® Update:
Locoregional Treatment Approaches for Hepatocellular Carcinoma

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National Comprehensive Cancer Network®

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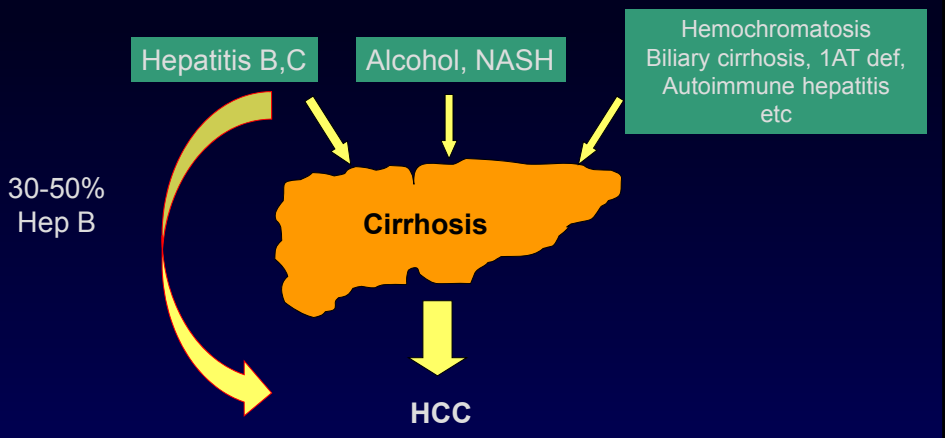
Locoregional Therapy in the Treatment of Hepatocellular Carcinoma

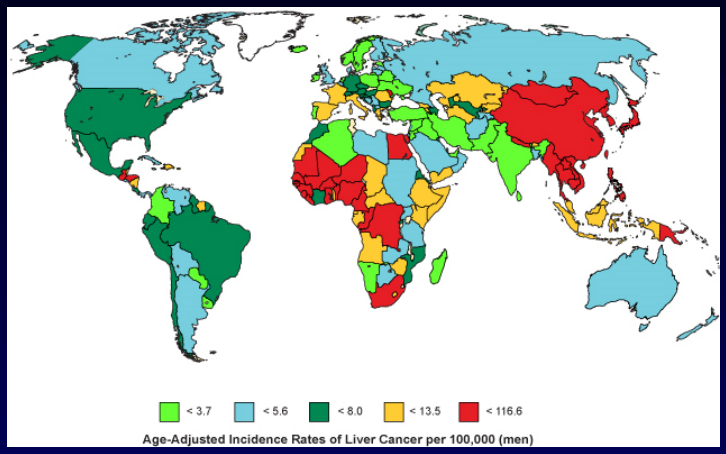
Anne M Covey, MD, FSIR
Member, Memorial Sloan Kettering Cancer Center
Associate Professor of Radiology, Weill Cornell Medical Center

Hepatocellular carcinoma most commonly occurs in the setting of underlying liver disease



The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hepatobiliary Cancers (Version 1.2016). © 2016 National Comprehensive Cancer Network, Inc.

Hepatocellular carcinoma is a global problem; the 5th most common cause of cancer worldwide and the 3rd leading cause of cancer related death



Aucejo F. Hepatocellular Carcinoma. *Cleveland Clinic Center for Continuing Education: Disease Management* 2013. Available at: http://bit.ly/1tfw8xa.

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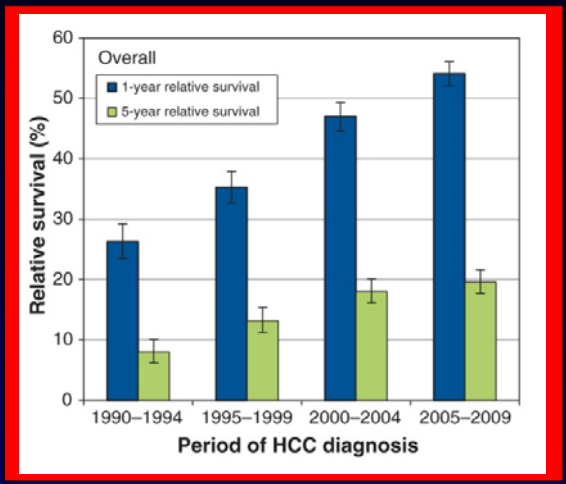

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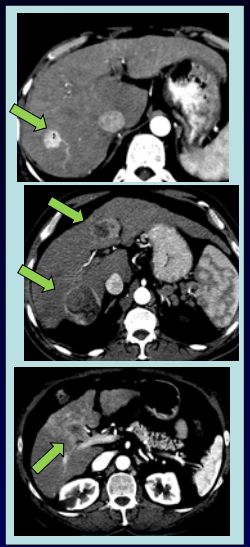
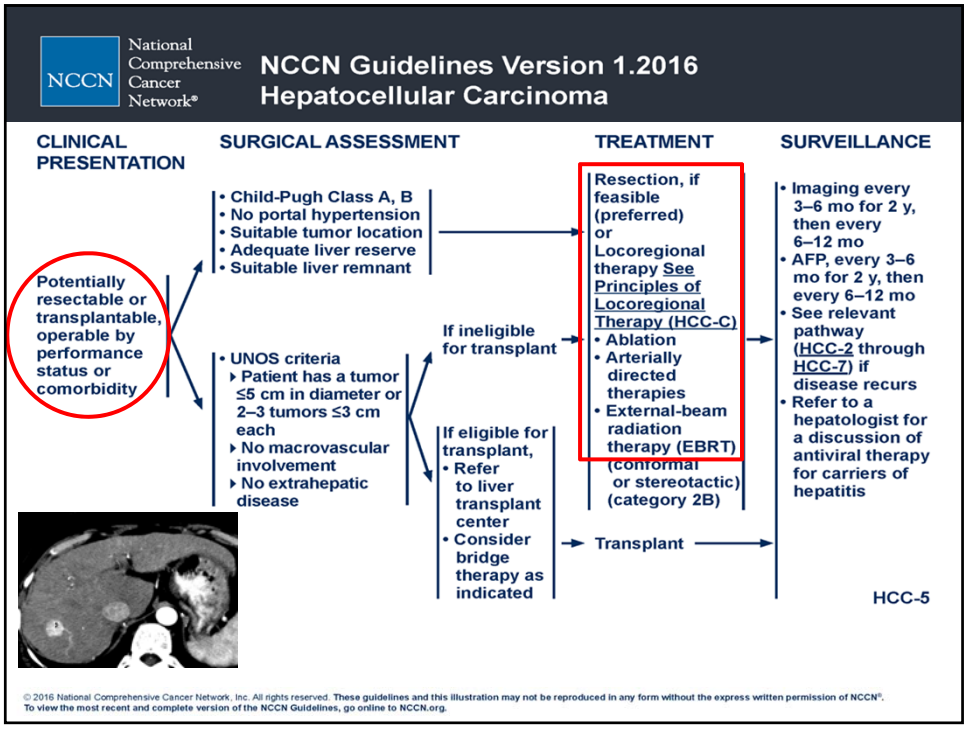
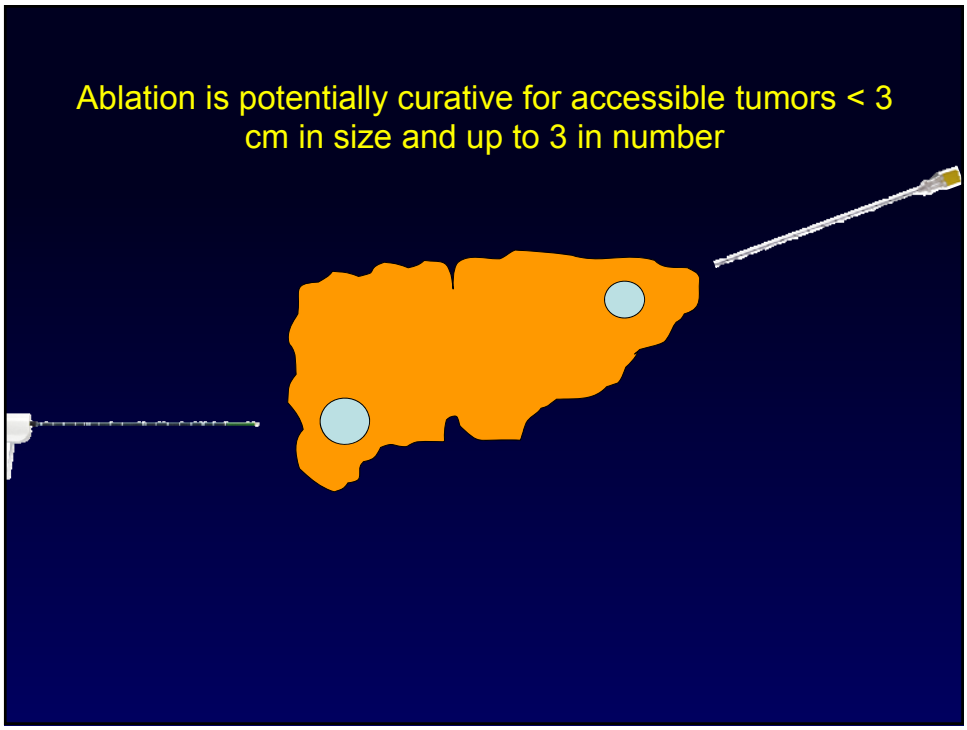
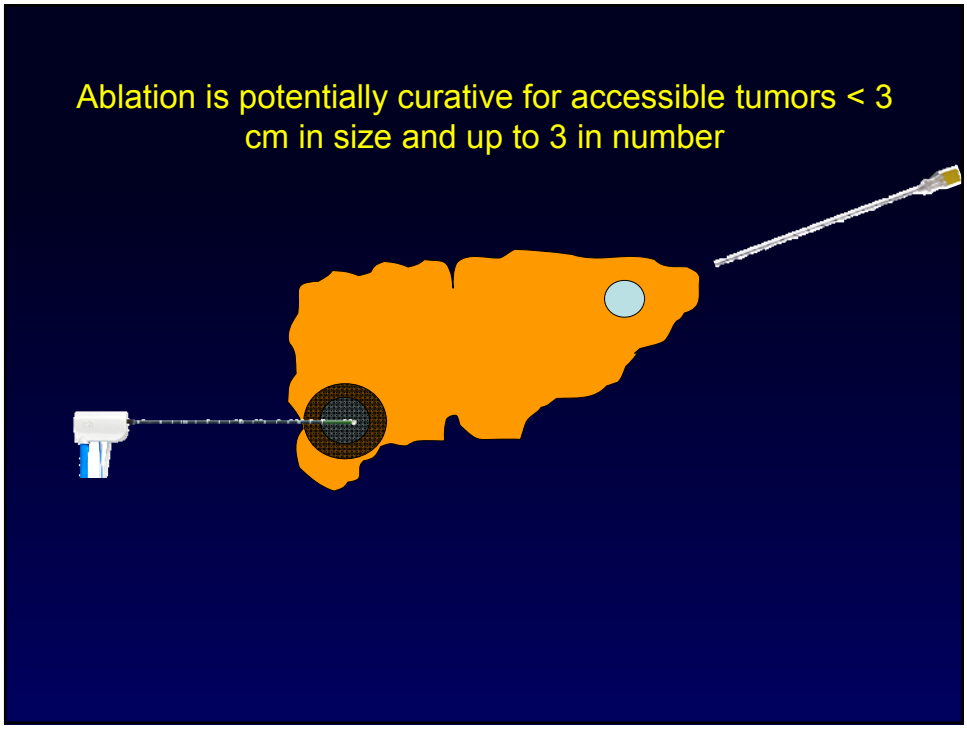
Treatment options depend on factors related to both tumor and underlying liver dysfunction

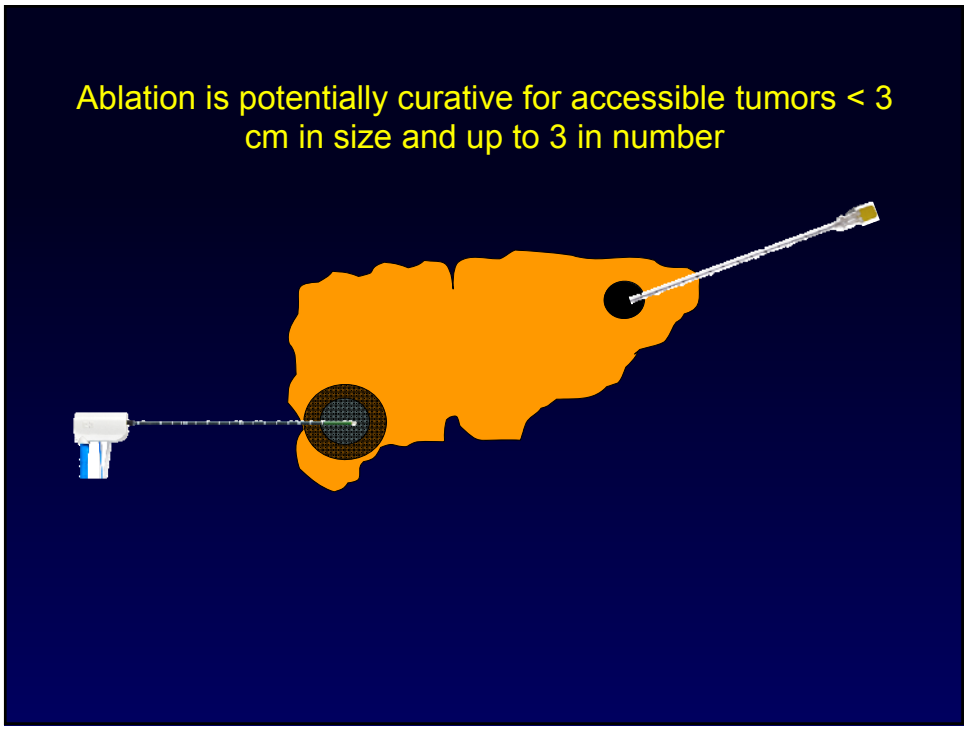


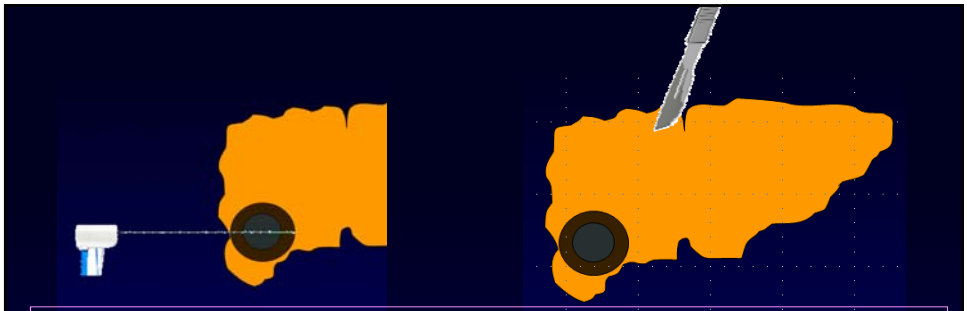
- 1-3 tumors < 3 cm → Resection, Transplantation, Ablation
- Multi-focal > 3 cm
- Liver dominant → Arterially directed therapy +/- ablation, Chemotherapy
- Extrahepatic dz
- Vascular invasion → Chemotherapy, Arterially directed therapy?











There are 4 RCTs and several NRCTs comparing RFA and surgical resection in the treatment of small HCC

For lesions < 3 cm overall survival at 1, 3, 5 years is no different

+ Less transfusion
+ Shorter hospital stay
- *Limited by tumor location*

+Lower rate of local recurrence
+Better long-term disease-free
-Increase risk of complications

Feng K et al. J. Hepatol 2013 57:794-802
Chen MS et al. Ann Surg 2006 243:321-328

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Randomized controlled trials comparing RFA to resection for HCC < 3 cm show no difference in 1, 3 & 4 year survival

Table 4. Summary of finding table for Solitary HCC with tumor size≤3 cm and 3–5 cm in RCTs.

				Event,%		Effect estimate#	
Indicators	Subgroup	Years	No. of Participants (studies)	RFA	HR	OR,95% CI	I^2 (%)
Overall survival	Tumor size≤3 cm	1-y	181(2)	93.6	97.7	0.49[0.03,8.45]	56
		3-y	181(2)	74.5	81.6	0.65[0.32,1.33]&	49
		4-y	181(2)	74.5	78.2	0.80[0.20,3.22]	73
	Tumor size 3~5 cm	1-y	153(2)	91.8	96.7	0.38[0.03,4.85]	54
		3-y	153(2)	62.3	83.7	0.26[0.05,1.36]	69
		4-y	153(2)	57.4	72.8	0.51[0.25,1.03]&	3

PLoS One. 2014 Jan 3;9(1):e84484. doi: 10.1371/journal.pone.0084484. eCollection 2014.

Radiofrequency ablation versus hepatic resection for small hepatocellular carcinomas: a meta-analysis of randomized and nonrandomized controlled trials.

Wang Y[1], Luo Q[2], Li Y[3], Deng S[4], Wei S[4], Li X[3].

Non-randomized controlled trials show significant benefit to resection probably due to patient selection bias

Table 6. Summary of finding table for HCC patients with tumor size ≤3cm in NRCTs.

				Event,%		Effect estimate#		
Indicators	Subgroup	Years	No. of Participants (studies)	RFA	HR	OR,95% CI	I^2 (%)	P value
	Single HCC	1-y	1516(8)	94.7	95.7	0.67[0.42,1.09]	9	0.11
		3-y	1516(8)	80.4	87.2	0.59[0.32,1.09]&	70	0.09
		5-y	1516(8)	64.3	77.9	0.52[0.31,0.87]&	74	0.01*

Table 5. Summary of finding table for HCC patients with tumor size between 3 and 5 cm in NRCTs

			Event,%		Effect estimate#		
Indicators	Years	No. of Participants (studies)	RFA	HR	OR,95% CI	I^2 (%)	P value
Overall survival	1-y	243(3)	95.4	92.9	1.62[0.54,4.84]	0	0.39
	3-y	243(3)	56.2	61.9	0.80[0.48,1.34]	0	0.40
	5-y	243(3)	26.2	45.1	0.43[0.25,0.73]	24	0.002*

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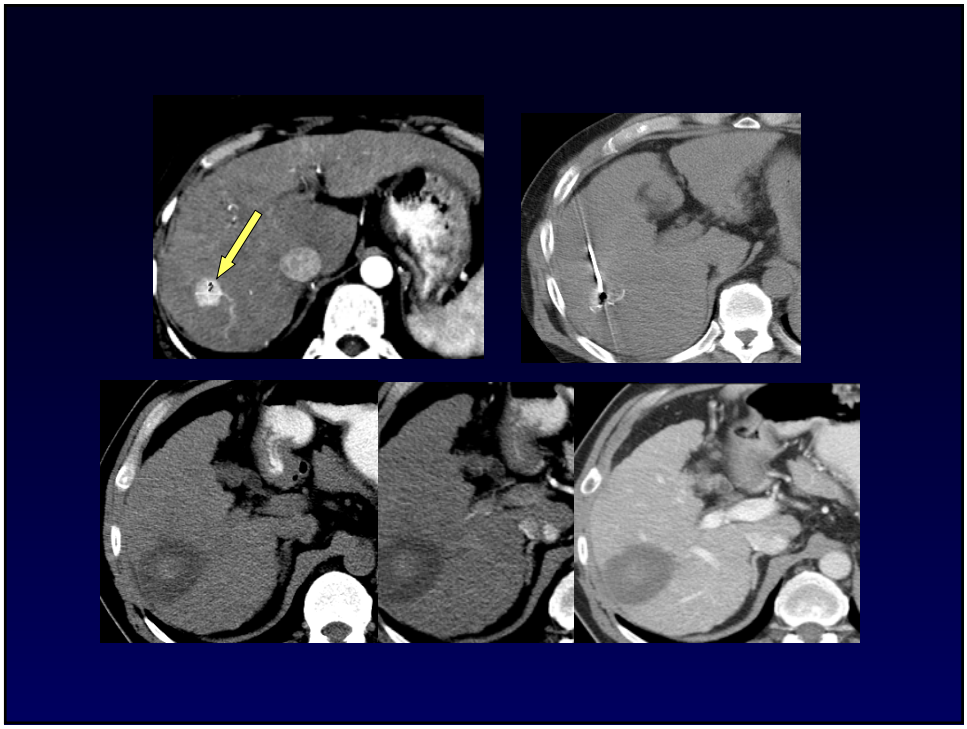
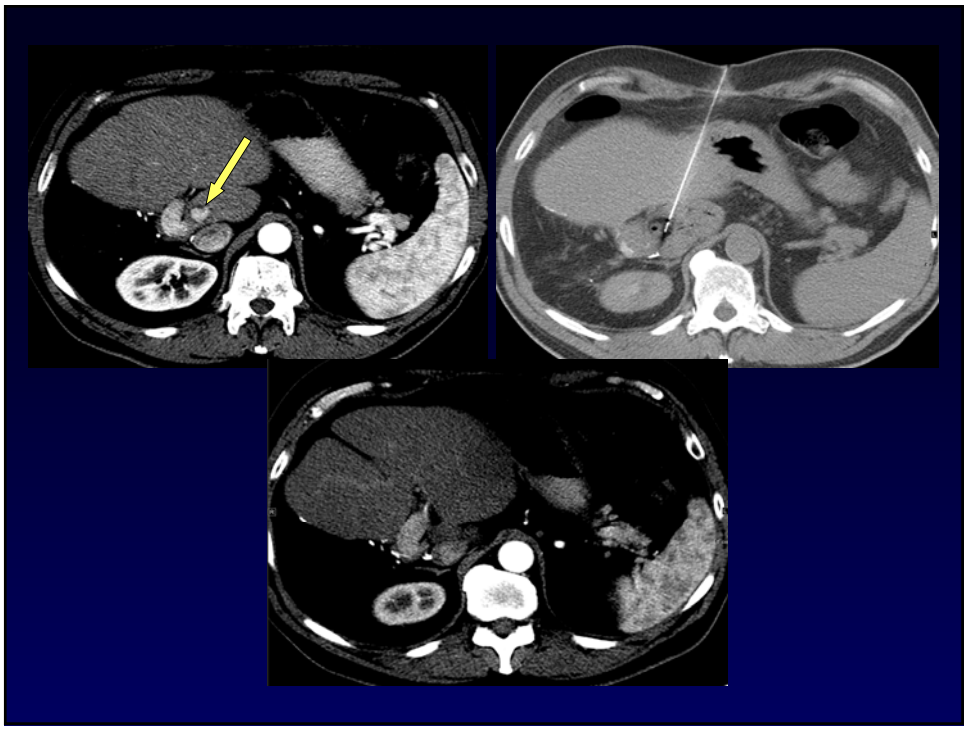
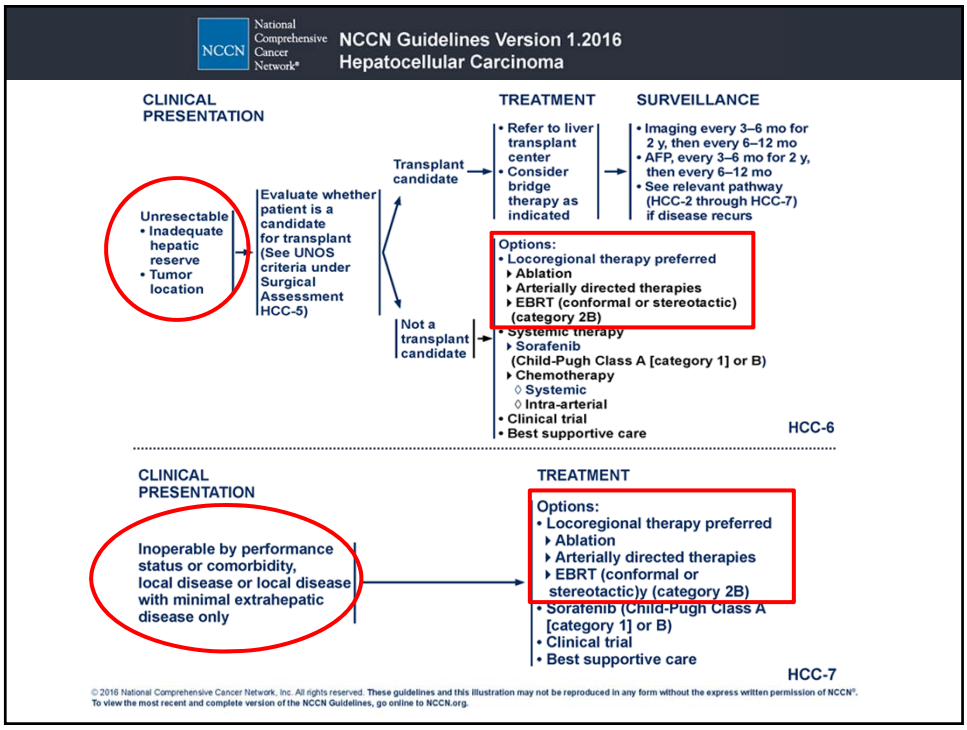


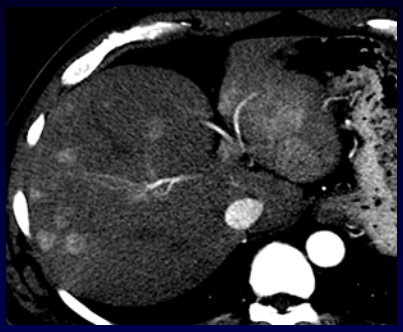


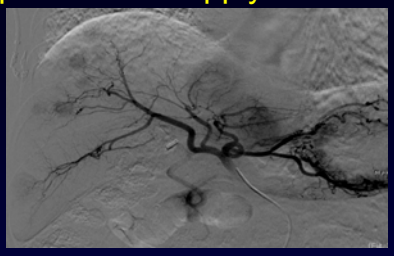
For resectable tumors, resection or transplant is preferred if feasible.

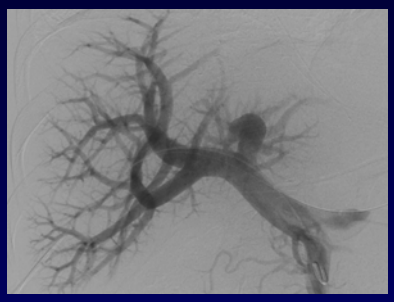
Ablation may also be curative for HCC < 3 cm.



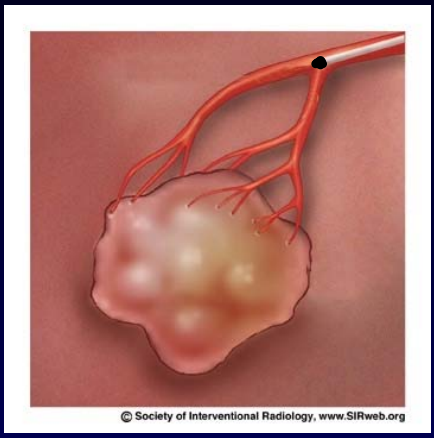
Arterially directed therapies to the liver are possible due to the dual nature of hepatic blood supply







Bland embolization (TAE, HAE)



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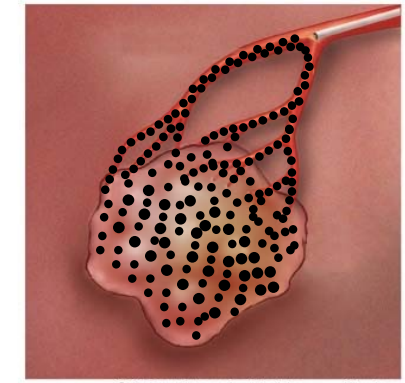

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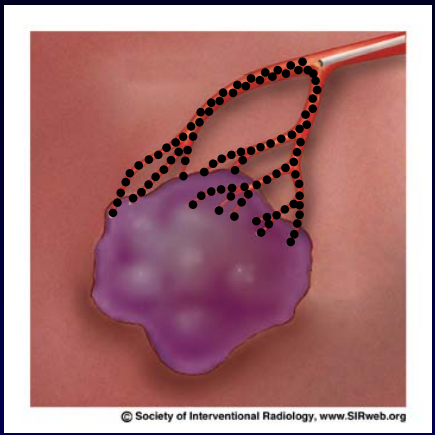
TAE



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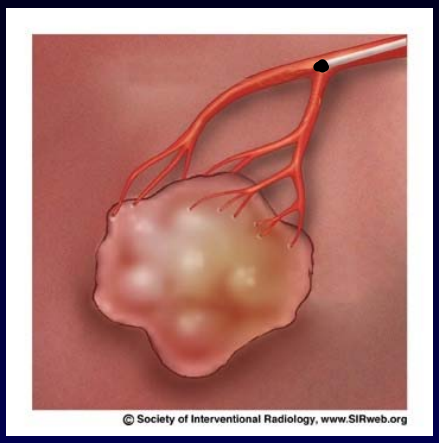
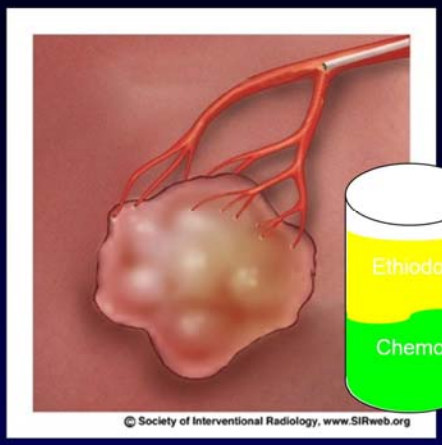


Transarterial chemoembolization (TACE)



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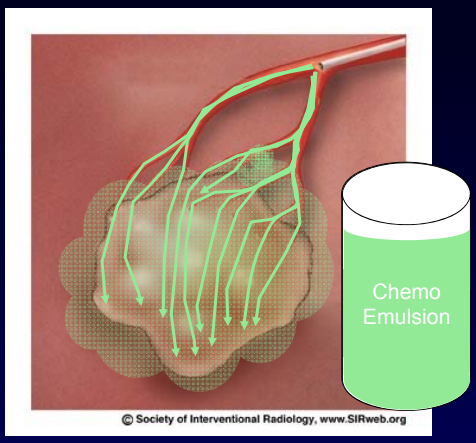

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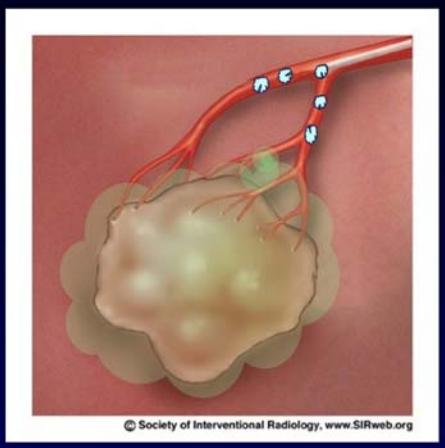

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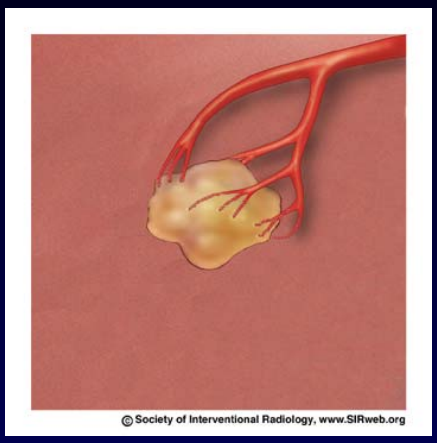
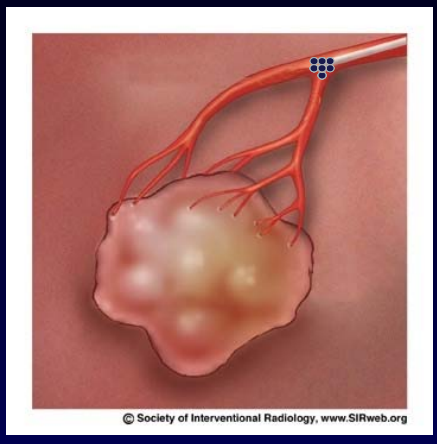


Embolization with drug eluting beads (DEB)



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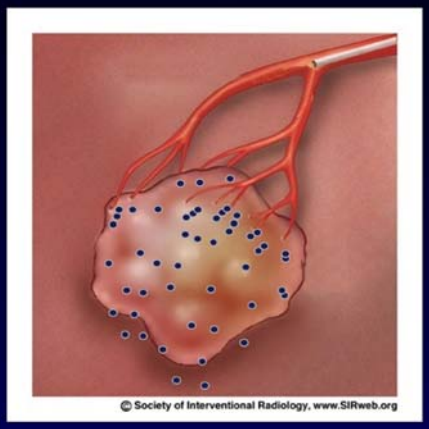

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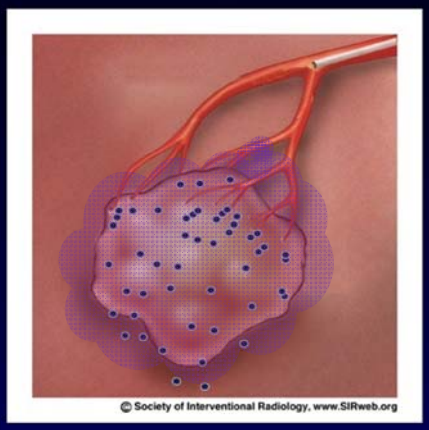
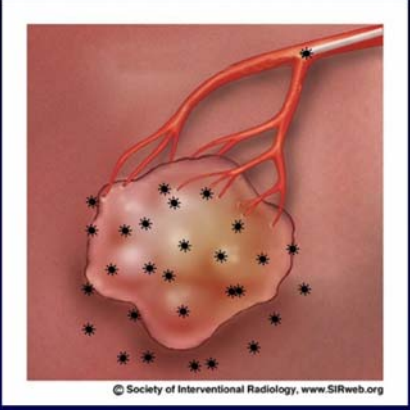


Embolization with drug eluting beads (DEB)

Radio “embolization” with Y90 (RAE)

^{90}Y RAE



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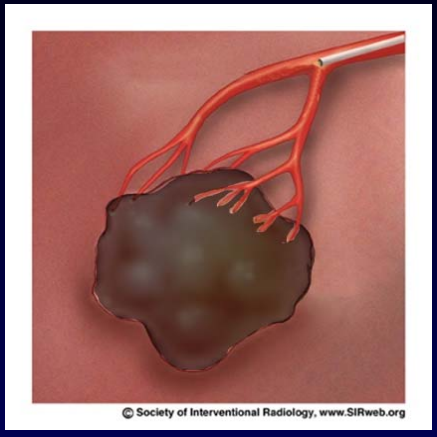
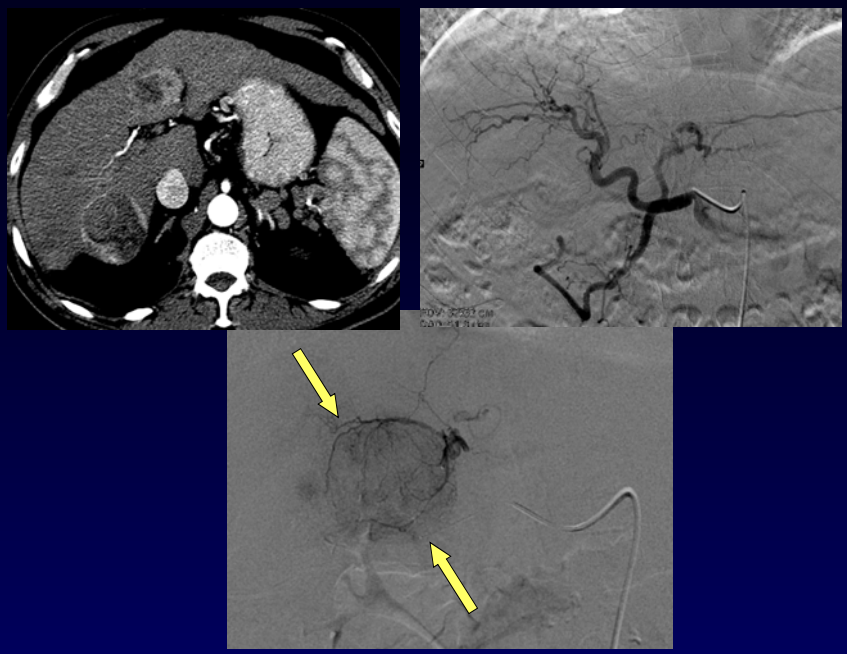
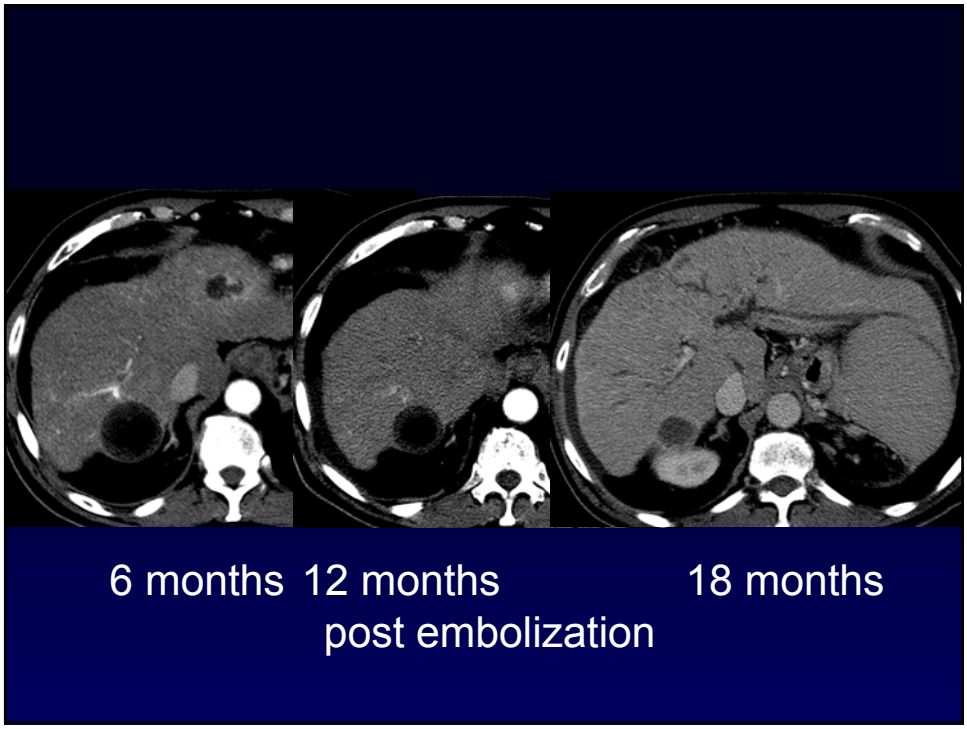
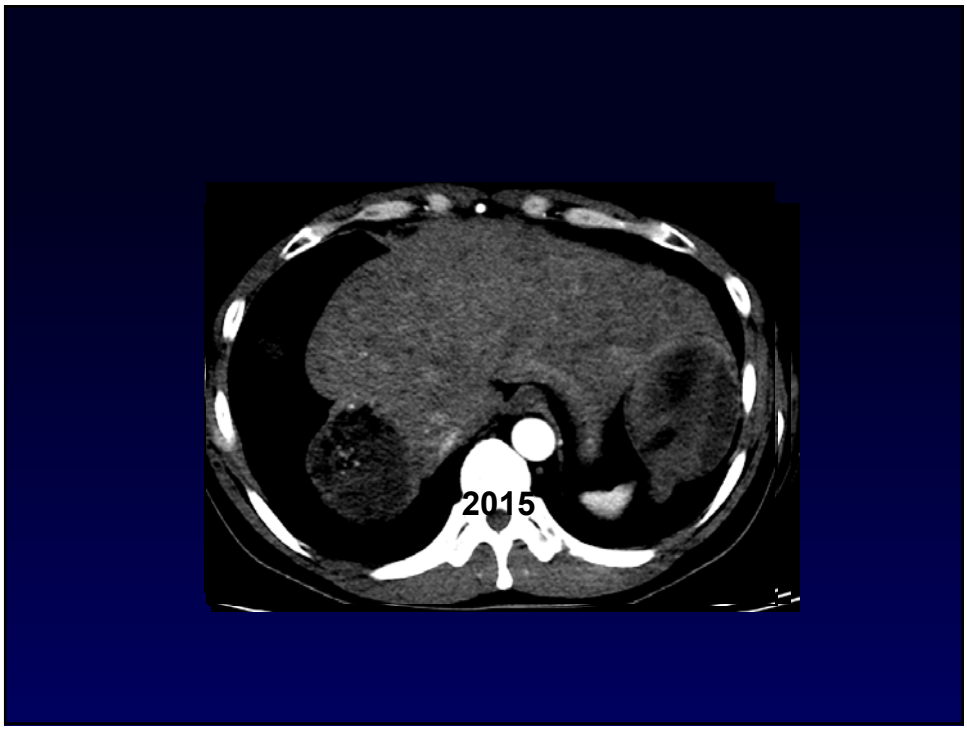
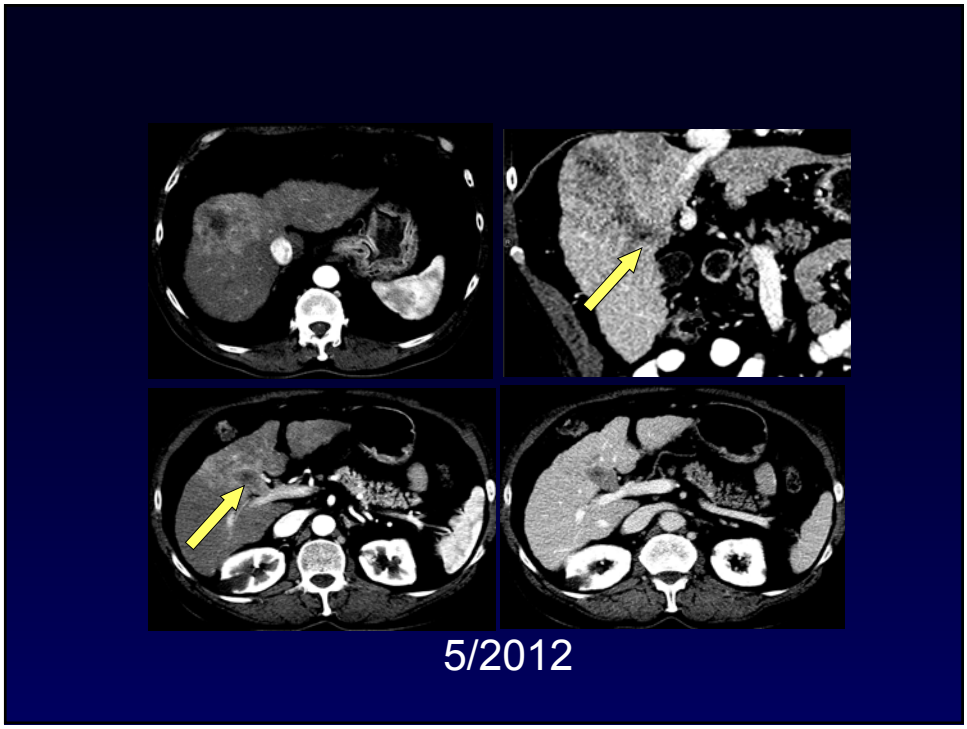
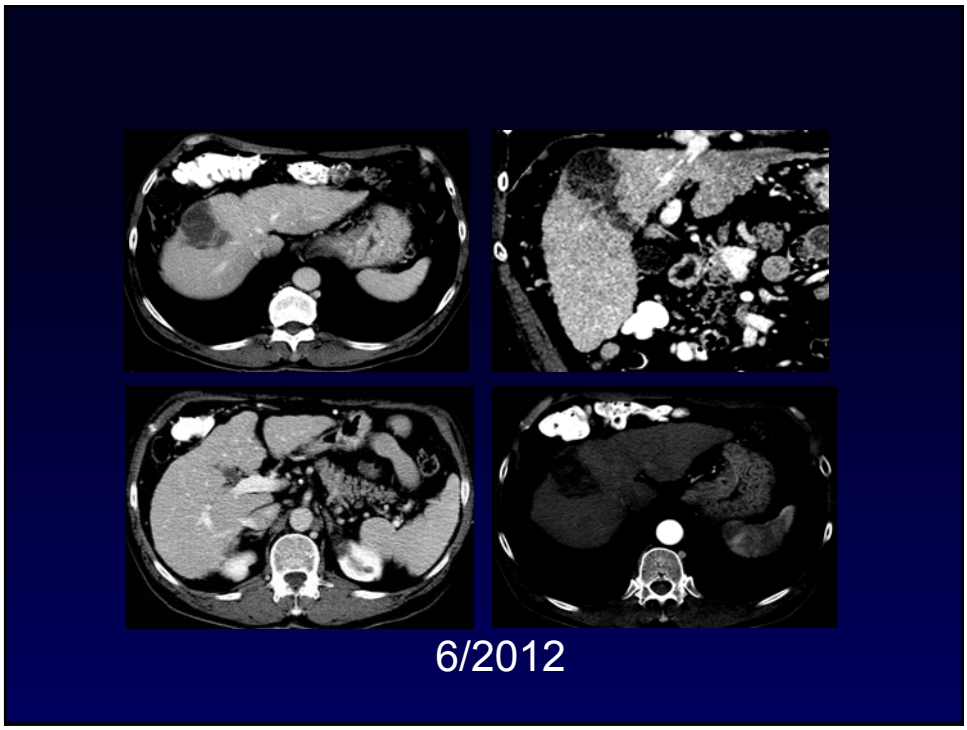




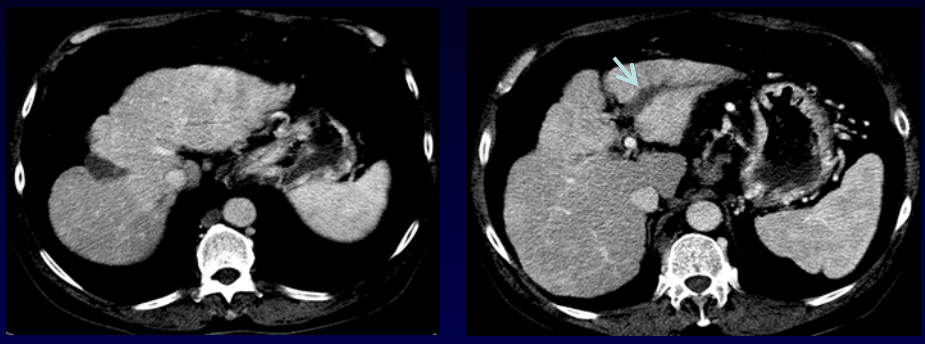






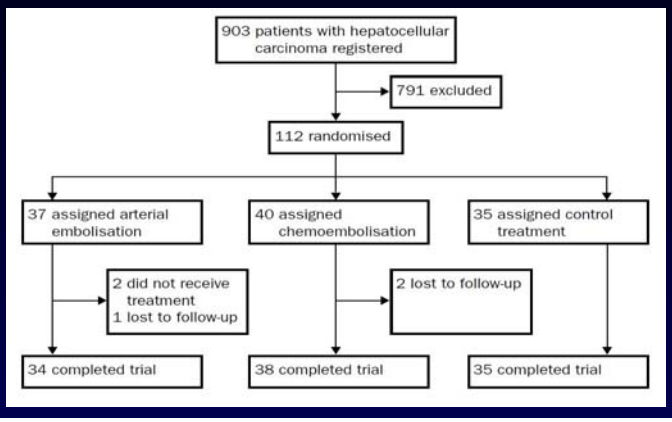


No additional treatment 6/2012-1/2014



1/2014

Two randomized controlled trials showing embolization has a survival advantage compared to best supportive care.



Lancet. 2002 May 18;359(9319):1734-9.

Arterial embolisation or chemoembolisation versus symptomatic treatment in patients with unresectable hepatocellular carcinoma: a randomised controlled trial.

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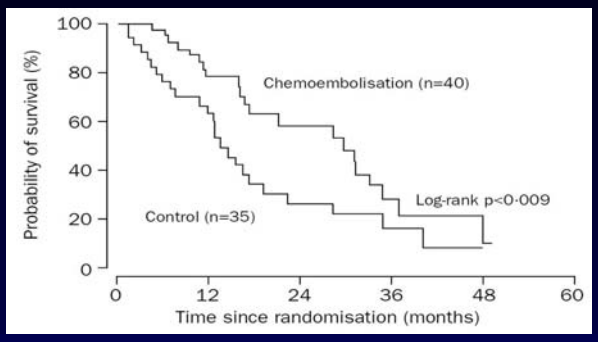

OS at 3 years in TACE vs supportive care 29 vs 17%

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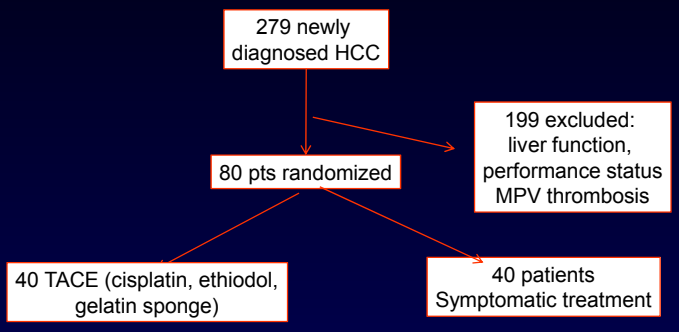

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Hepatology. 2002 May;35(5):1164-71.

Randomized controlled trial of transarterial lipiodol chemoembolization for unresectable hepatocellular carcinoma.

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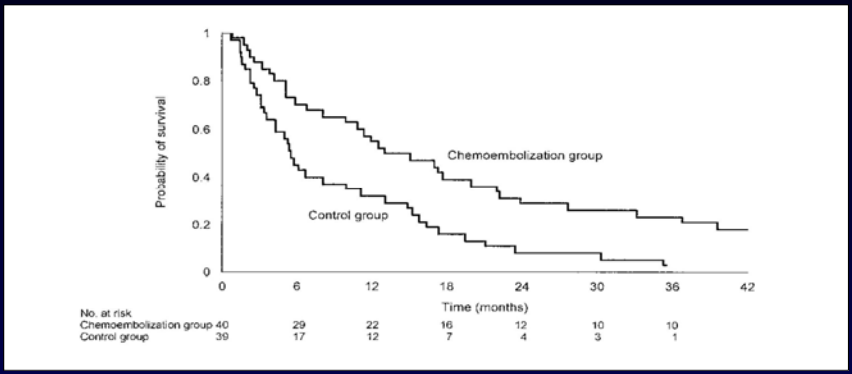

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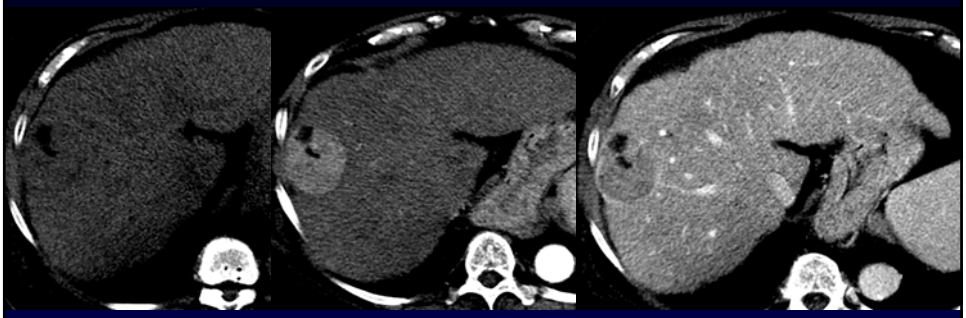
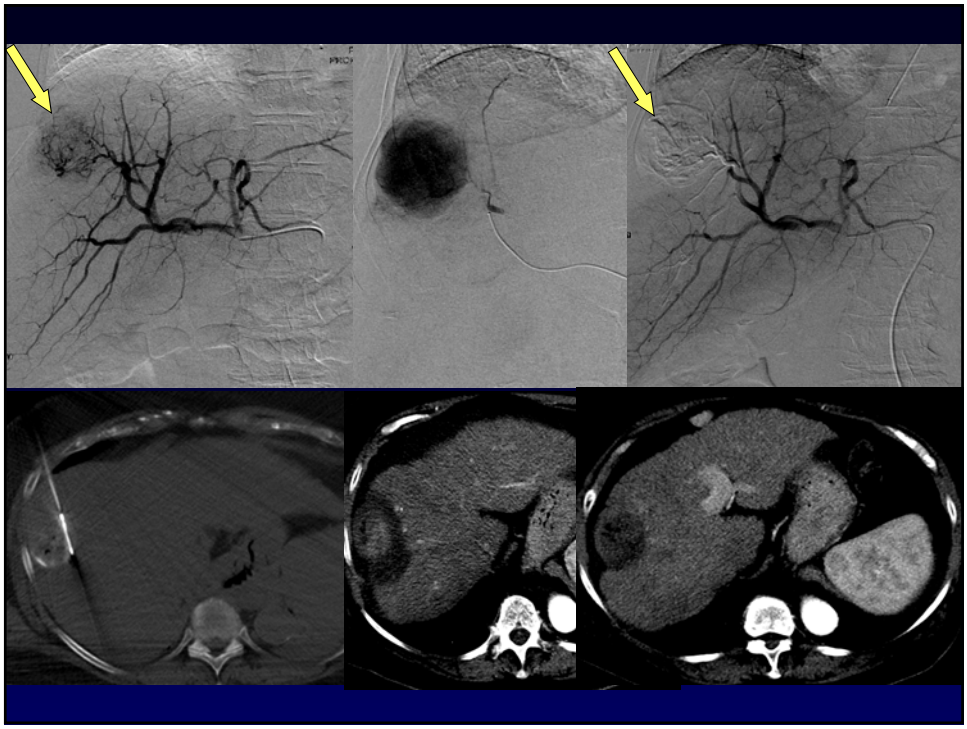
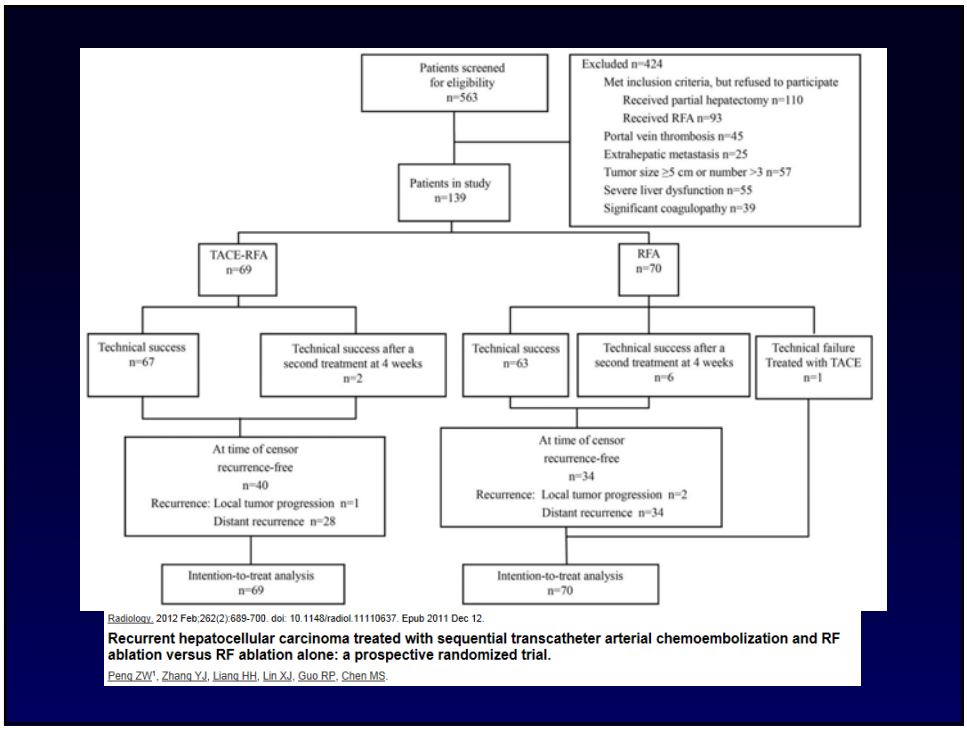
Combination of arterially directed therapy and ablation is recommended when there are 1-3 tumors 3-5 cm







Radiology. 2012 Feb;262(2):689-700. doi: 10.1148/radiol.11110637. Epub 2011 Dec 12.

Recurrent hepatocellular carcinoma treated with sequential transcatheter arterial chemoembolization and RF ablation versus RF ablation alone: a prospective randomized trial.

Peng ZW[1], Zhang YJ, Liang HH, Lin XJ, Guo RP, Chen MS.

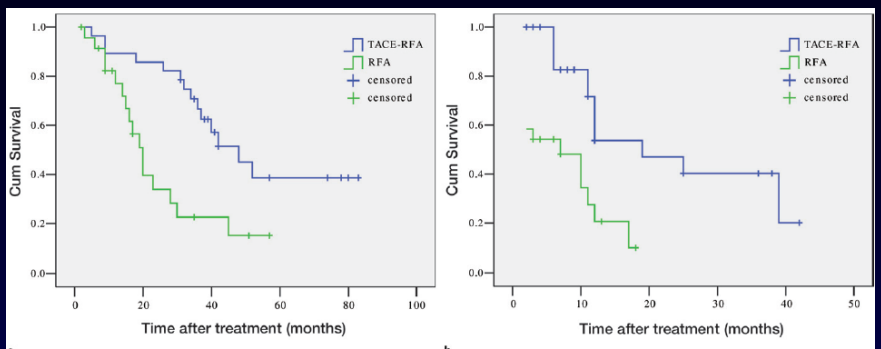
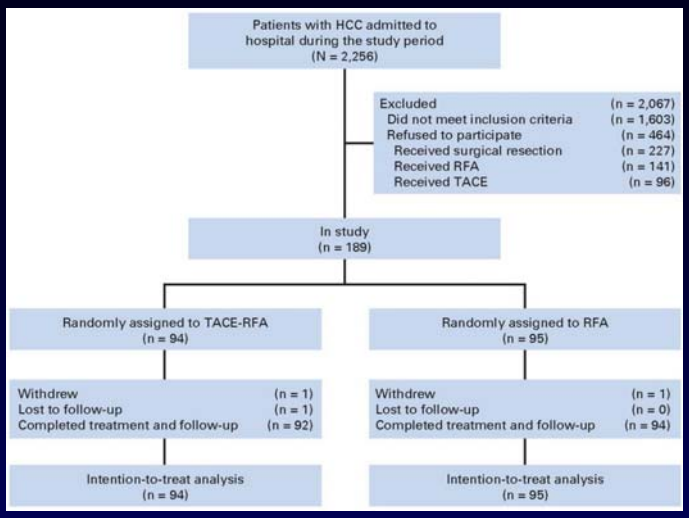


Figure 3: Cumulative (*Cum*) survival curves for subgroup analysis of patients with tumors measuring 3.1–5.0 cm. Curves show **(a)** overall and **(b)** recurrence-free survival for patients treated with sequential TACE-RF ablation and RF ablation alone.

Radiology. 2012 Feb;262(2):689-700. doi: 10.1148/radiol.11110637. Epub 2011 Dec 12.

Recurrent hepatocellular carcinoma treated with sequential transcatheter arterial chemoembolization and RF ablation versus RF ablation alone: a prospective randomized trial.

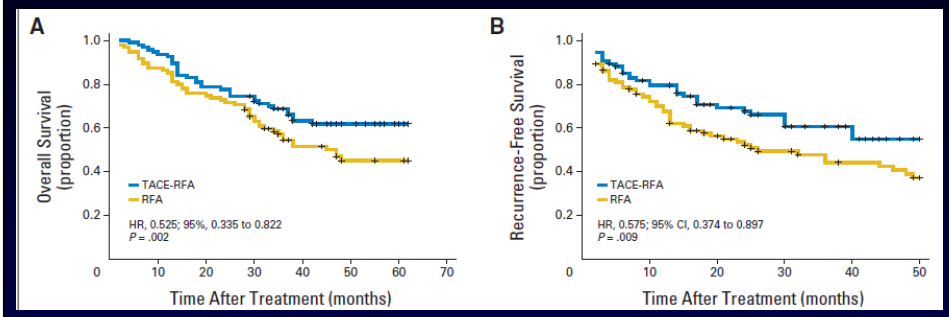
Peng ZW[1], Zhang YJ, Liang HH, Lin XJ, Guo RP, Chen MS.



J Clin Oncol. 2013 Feb 1;31(4):426-32. doi: 10.1200/JCO.2012.42.9936. Epub 2012 Dec 26.

Radiofrequency ablation with or without transcatheter arterial chemoembolization in the treatment of hepatocellular carcinoma: a prospective randomized trial.

Peng ZW[1], Zhang YJ, Chen MS, Xu L, Liang HH, Lin XJ, Guo RP, Zhang YQ, Lau WY.



J Clin Oncol. 2013 Feb 1;31(4):426-32. doi: 10.1200/JCO.2012.42.9936. Epub 2012 Dec 26.

Radiofrequency ablation with or without transcatheter arterial chemoembolization in the treatment of hepatocellular carcinoma: a prospective randomized trial.

Peng ZW[1], Zhang YJ, Chen MS, Xu L, Liang HH, Lin XJ, Guo RP, Zhang YQ, Lau WY.

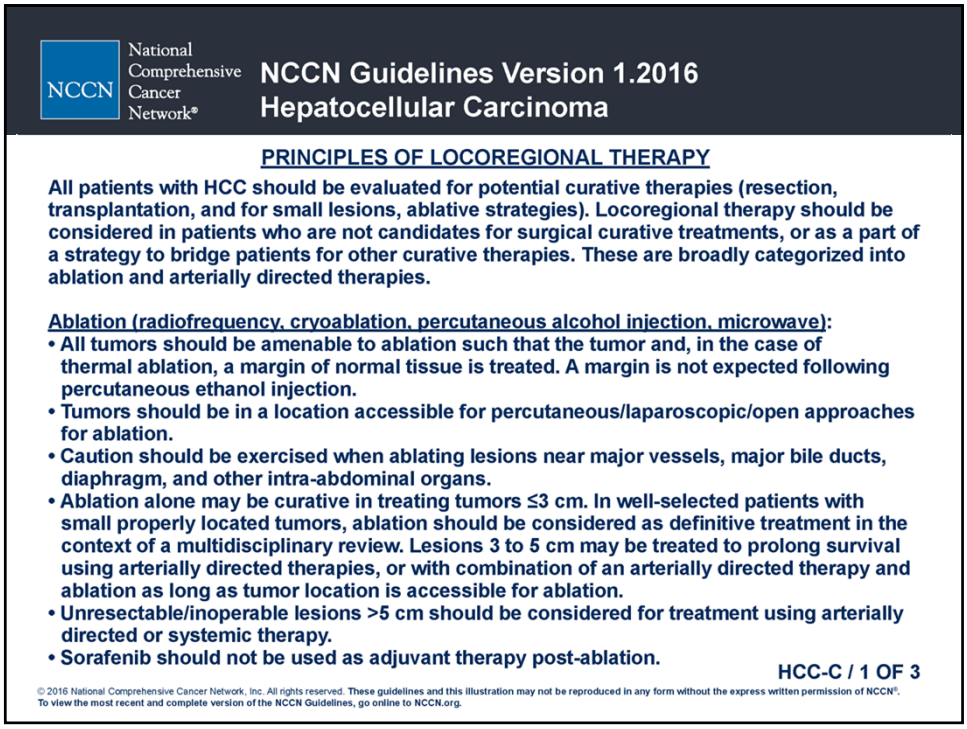
For unresectable tumors > 3 cm in patients with preserved liver function, treatment with arterially directed therapy is recommended.

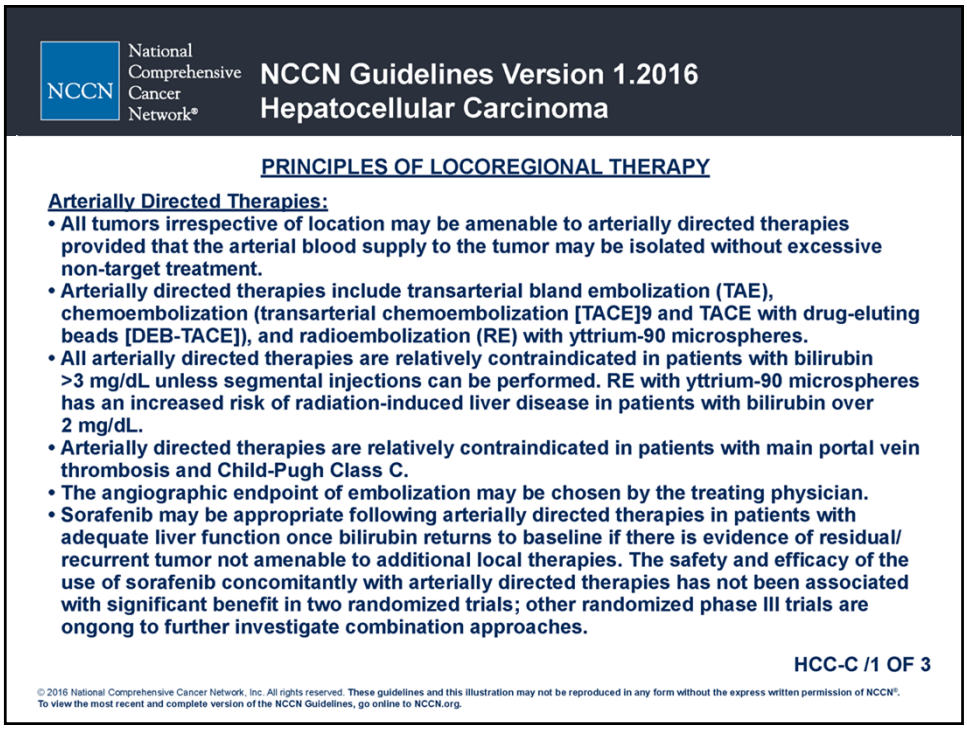
The choice of which arterially directed therapy is based on local expertise.

Combination arterially directed therapy and ablation may be used to treat tumors 3-5 cm.

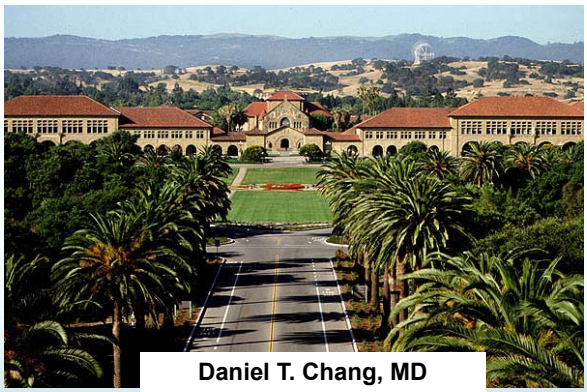
Locoregional therapy for HCC

- Ablation alone may be curative for small HCC < 3 cm
- Arterially directed therapies are recommended for unresectable lesions > 3 cm
  - TAE/HAE, TACE, DEB, RAE
  - Specific treatment usually dictated by local expertise
- Combination arterially directed therapy and ablation is recommended for patients with 1-3 tumors 3-5 cm
- Sorafenib is reserved for residual/recurrent tumor not amenable to additional local therapy



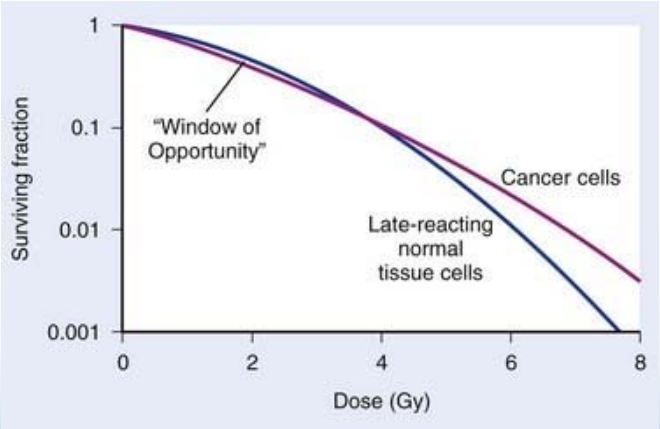


Updates on Local-Regional Therapy for Hepatocellular Carcinoma: External Beam Radiation

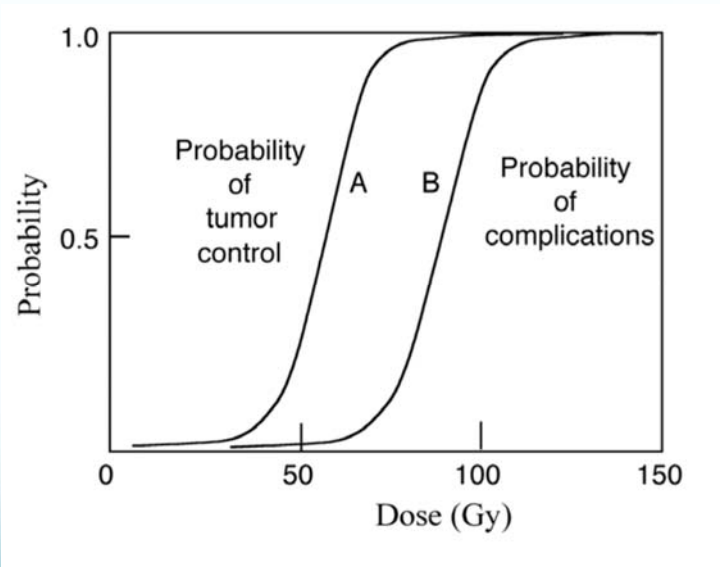


Daniel T. Chang, MD
Radiation Oncology
Associate Professor
Stanford University

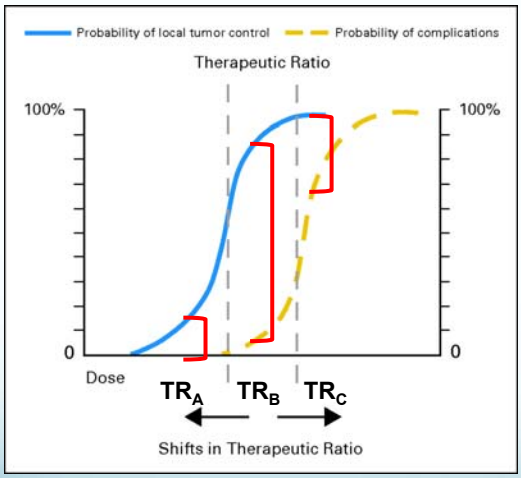
Basics of Radiobiology



Nag, S., et al. "High Dose Rate Brachytherapy", 2015.



Podgorsak, Review of Radiation Oncology Physics: A Handbook for Teachers and Students. IAEA 2005



Therapeutic Ratio

TR = prob tumor control / prob toxicity

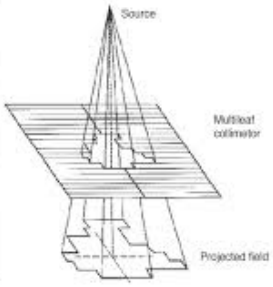
Optimize Ther Ratio

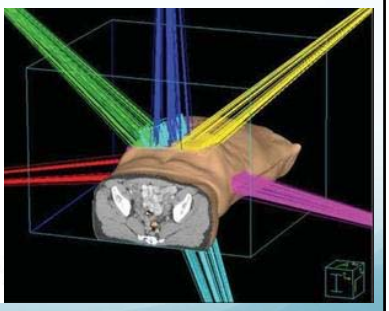
$TR_B >> TR_A$ and TR_C

Brizel, D Pharmacologic Approaches to Radiation Protection JCO 2007

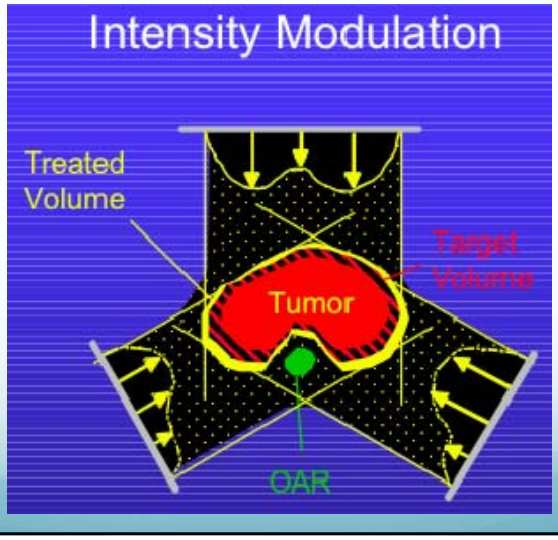
Terms and Definitions

- EBRT – external beam radiotherapy
  - Radiation that comes from a machine into the patient
  - Photons or electrons, protons, heavy ions
- 3D CRT – 3D conformal RT
  - CT-based planning using uniform beams to treat a target

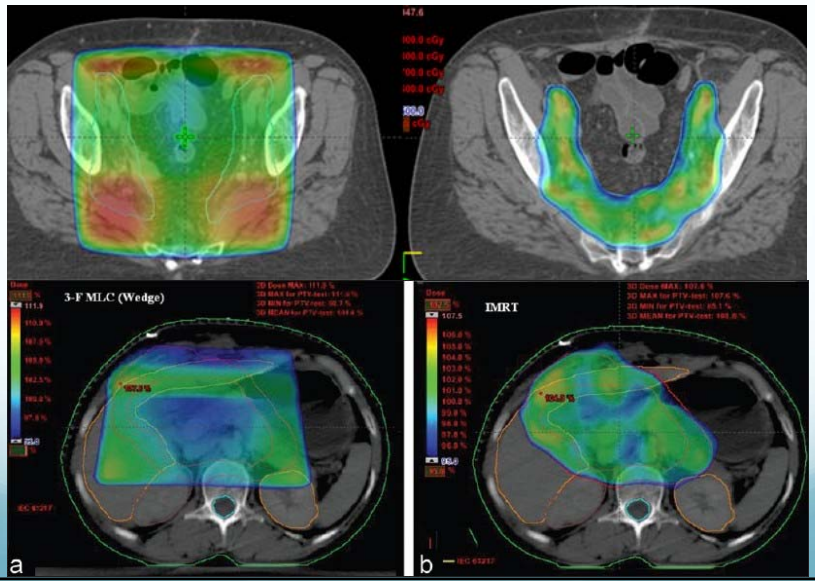




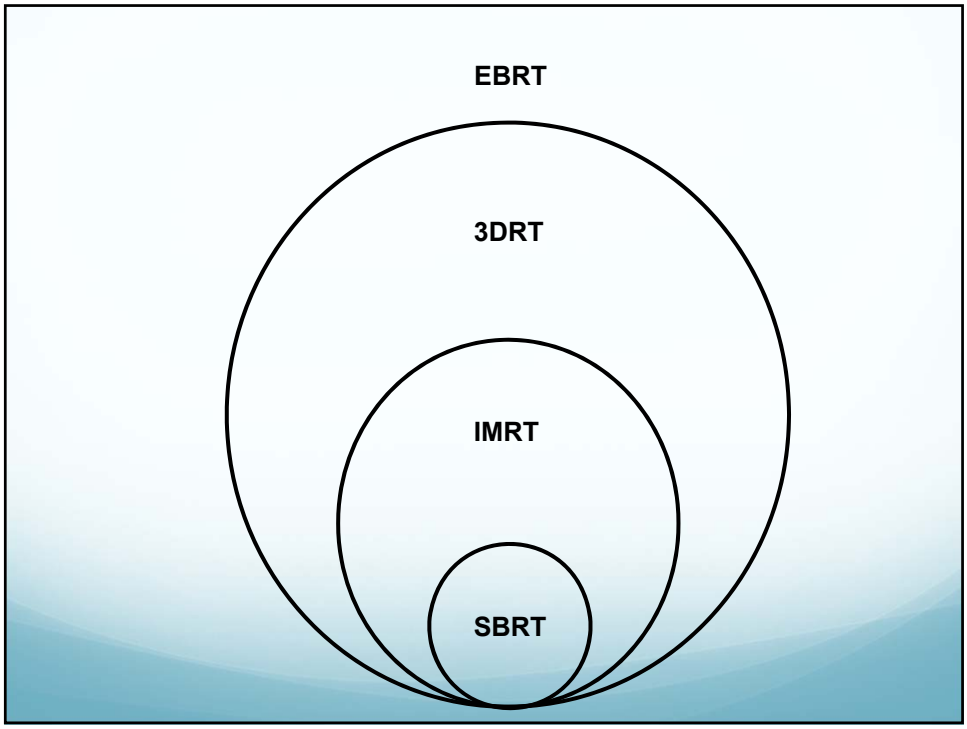
- IMRT – intensity modulated radiotherapy
  - Advanced conformal radiation using non-uniform beam intensities to shape the dose around critical structures



3D RT vs IMRT



- SBRT – stereotactic body radiotherapy
  - SABR – stereotactic ablative radiotherapy
  - High doses of radiation (8-25 Gy/day), usually with IMRT, delivered in ≤5 fractions
  - Ablative compared with conventional fractionation (2 Gy/day)
- IGRT – image guided radiotherapy
  - Any of the above using kV imaging to ensure target alignment

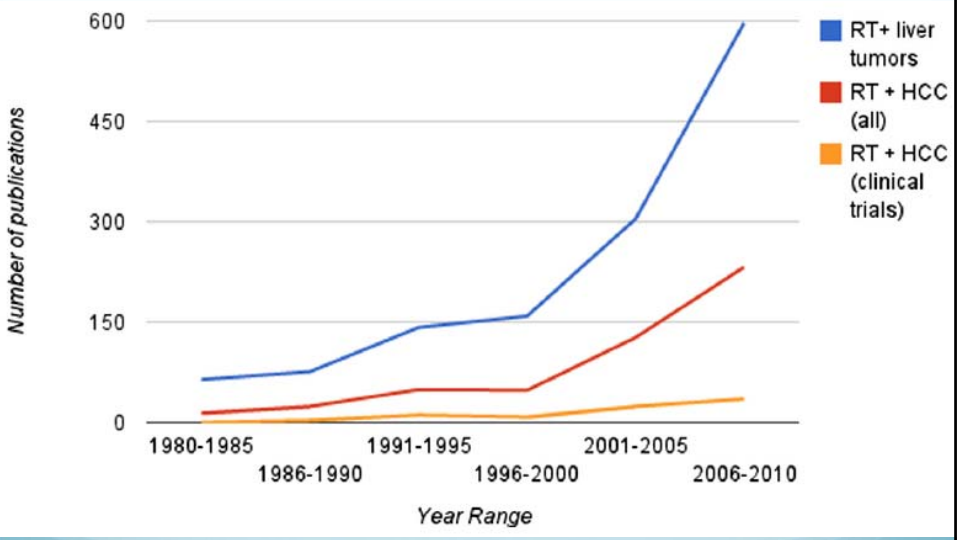


What's in a name?

Liver Radiotherapy

- Historically not used due to concerns of toxicity of liver radiation
  - 1965 paper from Stanford first described radiation hepatitis
- RT primarily reserved for palliation
- Development of 3-D radiation and recognition that partial liver volumes could tolerate higher doses of radiation (>30 Gy) lead to expanded use of liver radiotherapy

Ingold JA, Reed GB, Kaplan HS, et al: Radiation hepatitis. Am J Roentgenol Radium Ther Nucl Med 93:200-208, 1965
Reed GB Jr, Cox AJ Jr: The human liver after radiation injury. A form of veno-occlusive disease. Am J Pathol 48:597-611, 1966



Klein IJROBP 2013

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2016
Hepatocellular Carcinoma

CLINICAL PRESENTATION

TREATMENT

Inoperable by performance status or comorbidity, local disease or local disease with minimal extrahepatic disease only →

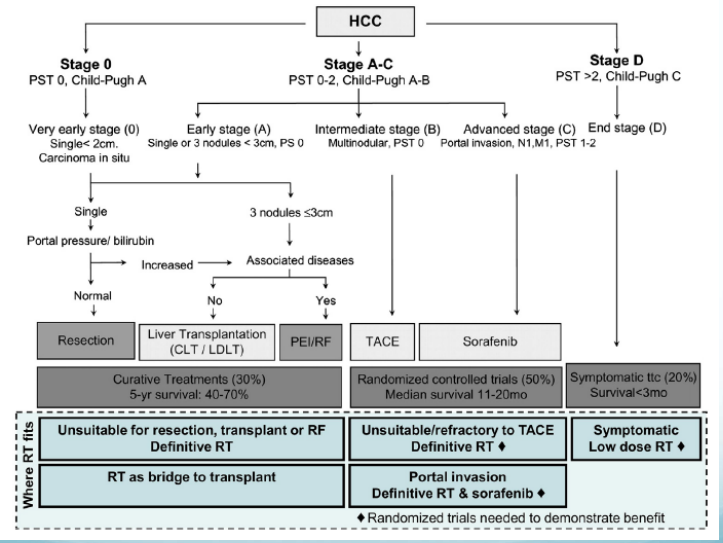
Options:
- **Locoregional therapy preferred**
  - **Ablation**
  - **Arterially directed therapies**
  - **EBRT (conformal or stereotactic)y (category 2B)**
- **Sorafenib (Child-Pugh Class A [category 1] or B)**
- **Clinical trial**
- **Best supportive care**

Metastatic disease or Extensive liver tumor burden → **Consider biopsy to confirm metastatic disease** →

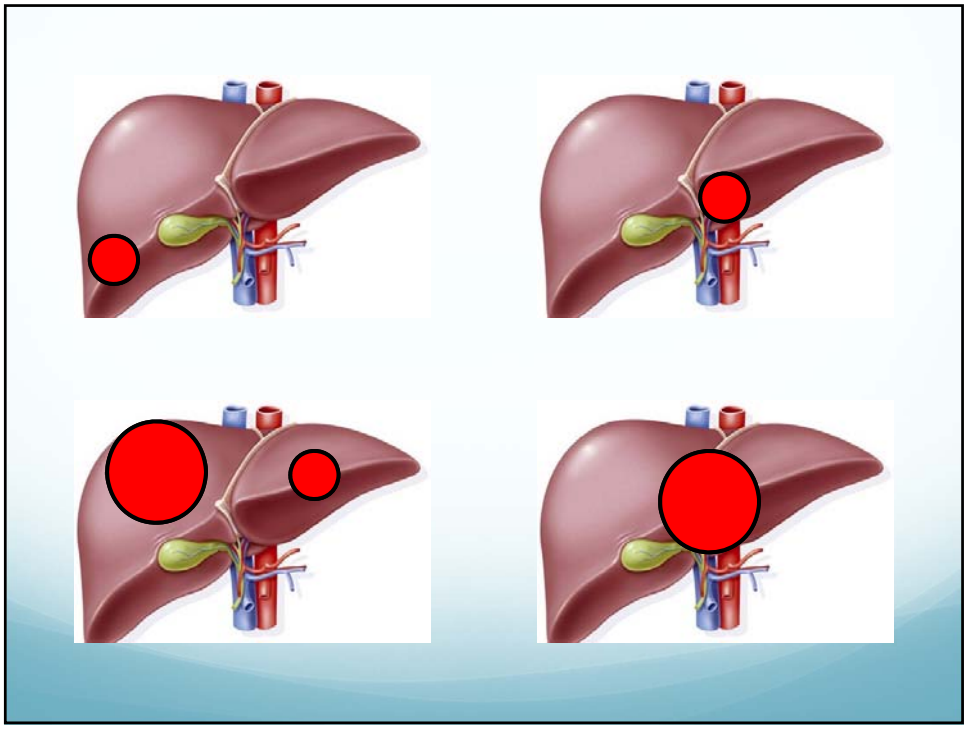
Options:
- **Sorafenib (Child-Pugh Class A [category 1] or B)**
- **Clinical trial**
- **Best supportive care**

HCC-7

Where does RT fit?



Klein IJROBP 2013

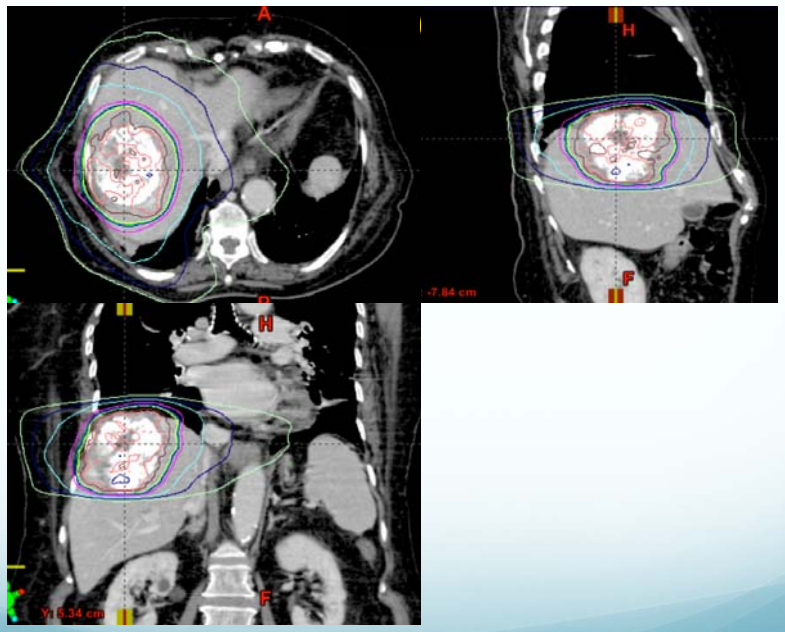


Take home points about radiation

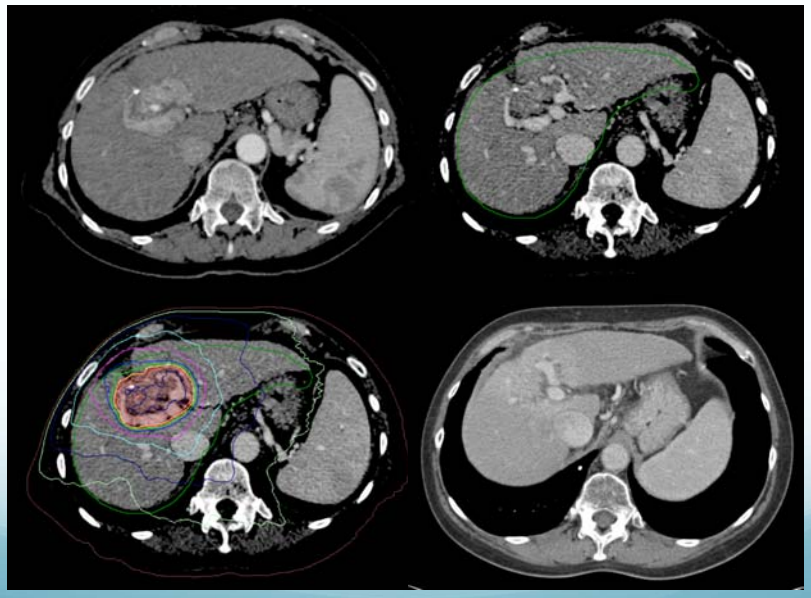
- Radiation is non-invasive
- No such thing as “too big,” though smaller is easier than bigger
- Can treat multiple tumors
- Dose can be adjusted based on size and location of critical structures
- Tumor thrombus is not a contraindication for treatment
- Caution about combining radiation with radioembolization

Combination of EBRT and Transarterial Chemoembolization (TACE)

- TACE with EBRT for salvage
- TACE combined with EBRT to treat the whole tumor
- TACE combined with EBRT to treat portal vein tumor thrombus

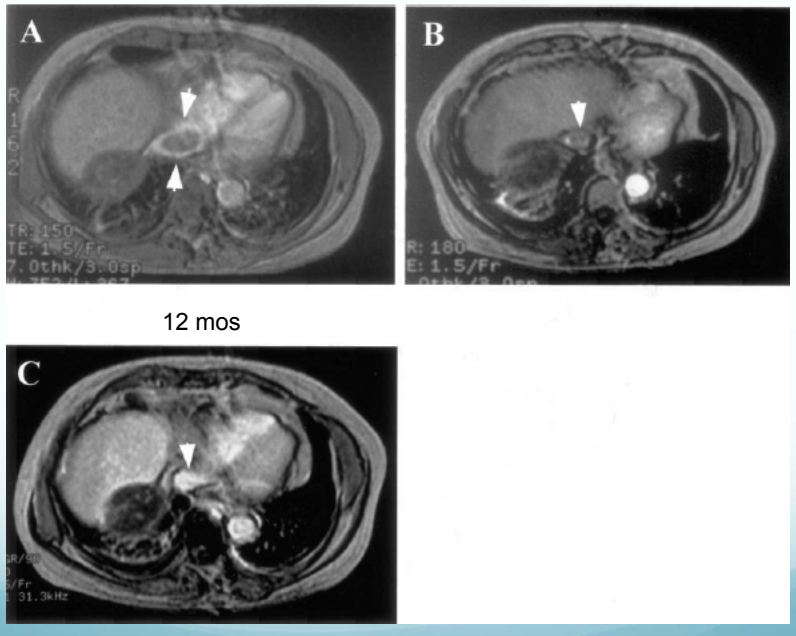


PVTT



Baseline

3 mos

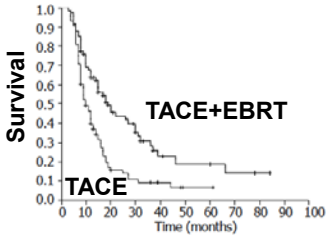


12 mos

Comparison between chemoembolization combined with radiotherapy and chemoembolization alone for large hepatocellular carcinoma

Guo World J Gastroenterol 2003

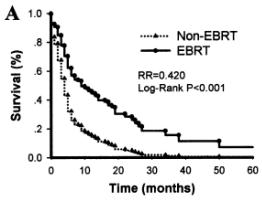
- HCC ≥5 cm, 22% with PVTT
- 76 pts – EBRT and TACE
- 89 pts – TACE alone
- ORR – 47% vs 28%, p<0.05



A comparison of treatment combinations with and without radiotherapy for hepatocellular carcinoma with portal vein and/or inferior vena cava tumor thrombus

Zeng IJROBP 2005

- PVTT or IVC thrombus
- 44 pts – EBRT and TACE
- 73 pts – TACE alone
- 18 pts – Surgery alone
- 23 pts – No therapy
- 34% CR of PVTT or IVCT with EBRT



Studies using EBRT

Series	Pts	CP Class A (%)	Tumor Size (Diameter or Volume)	PVT (%)	Total Dose, Dose per Fraction	1-Year LC (%)	1-Year OS (%)
Ben-Josef et al[16]	35	100	0.15-1,100 mL	0	40-90 Gy in 1.5 Gy twice daily	81	57
Mornex et al[18]	27	59	1-5 cm	NA	36-66 Gy in 2-Gy fx	78	NA
Liu et al[22]	44	86	<5 cm in 36 5-10 cm in 36, >10 cm in 27	32	40-60 Gy	61	61
Liang, et al[21]	128	84		29	38-68 Gy in mostly 4- to 6-Gy fx	69 at 3 mo	65
Kim et al[49]	70	88	Median 7.5 cm (2-17 cm)	59	44-54 Gy in 2- to 3-Gy fx	54 CR+PR	43
Oh et al[50]	40	90	1.5-23 cm	10		63 CR+PR	72
Seong et al[20]	398	77	1-23.8 cm	27	25-60 Gy in mostly 1.8- to 5-Gy fx	NA	45
Seo et al[30]	65	66	Median 9.9 cm	69	61 Gy in 1.8-Gy fx in 85% of patients	Median TTP 4 mo	35

Studies using EBRT with TACE

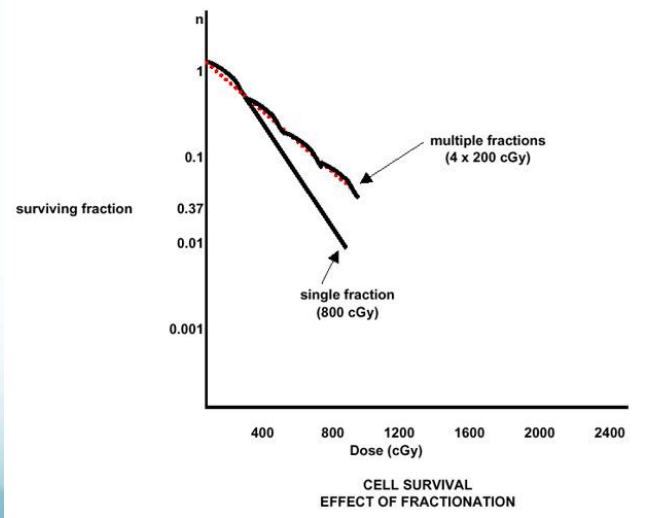
Study	Mean Tumor Size (range)	PVT (%)	No. of Patients	Treatment	Response CR (%)	Response PR (%)	Response SD (%)	Median Survival (months)
Li et al[20]	8.5 cm (4-13)	15 (33)	45	TACE + 50.4 Gy	6 (13)	35 (78)	4 (9)	23
Zeng et al[19]		0 (0)	54	TACE + 36-60 Gy	3 (6)	38 (70)	13 (24)	20
Seong et al[18]	9.0 cm (6-12)	80 (51)	158	TACE + 48.2±7.9 Gy	1 (1)	105 (67)	41 (26)	10
Guo et al[21]	10.2 cm (5-18)	23 (21)	107	TACE + 25-55 Gy	6 (6)	46 (43)	42 (39)	18

Feng and Ben-Josef Sem Radiat Oncol 2011

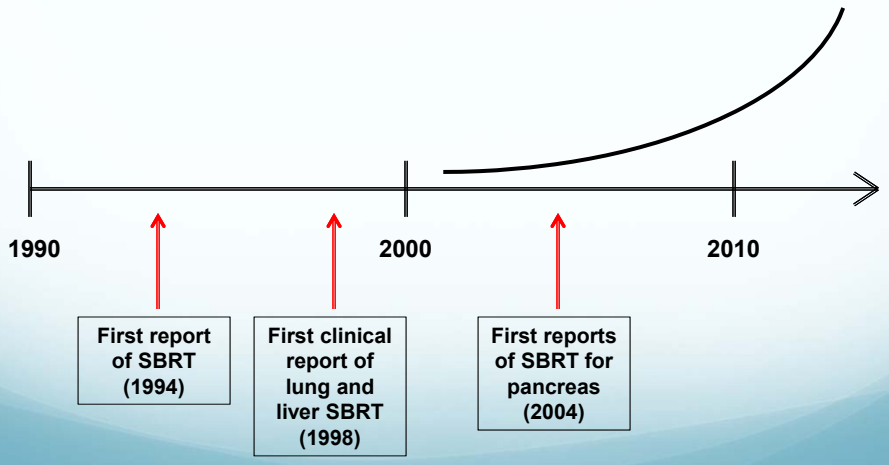
Potential Advantages of SABR/SBRT

- Improvement in local control
- Shorter course of treatment
  - Allows integration with more intensive systemic chemotherapy
  - Patient convenience
- Cost effective
- QOL

Model for Radiation Cell Killing



Stereotactic Body Radiotherapy (SBRT) Stereotactic Ablative Radiotherapy (SABR)



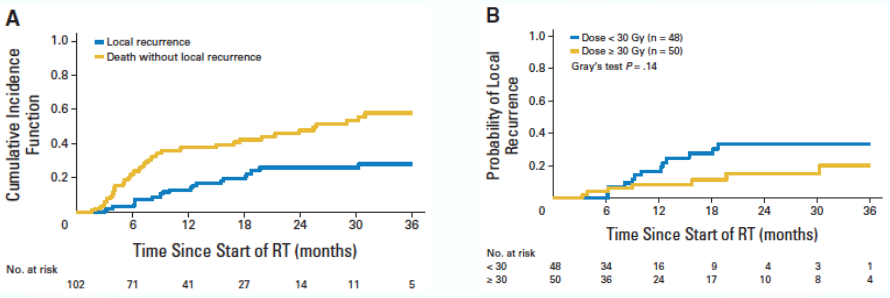
HCC SBRT Reports

	Patients	Lesions	SBRT	PTV	% Childs A/B	Local Control
Ibarra (2012)	32 21-HCC 11 - IHC	43	30-37.5 Gy/3 22 Gy/1 47 Gy/10	GTV + 3-5mm or 7-10(sup-inf)	CS 6-8	83% - 6 months 64% - 12 months
Andolino (2011)	60	71	30-48 Gy/3 – CPA 40 Gy/5 - CPB	GTV + 5axial, 10sup-inf	60/40	90% - 2 years
PMH	41	31 HCC 10 IHC	Variable, NTCP-based Median 6 Gy x 6	GTV+8mm+margin PTVprimary = GTV+5+mm	100/0	65% - 12 months
Choi (2008)	31	32	30-39 Gy/3	GTV + 5 mm	84/16	90% - crude
Seo (2010)	38	47	30-57 Gy/3	ITV + 2 mm axial, 4 mm sup-inf	89/8	78% - 12 months 66% - 2 years
Japan (Takeda)	16	16	20-50 Gy in 5-8 fractions	ITV + 5-10 mm	88/12	94% - crude

Sequential Phase I and II Trials of Stereotactic Body Radiotherapy for Locally Advanced Hepatocellular Carcinoma

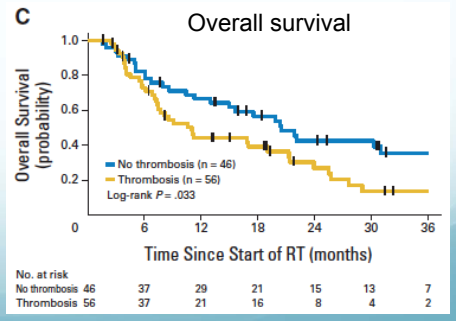
- 102 patients from 2 prospective trials
- All with Child Pugh A
- 38% with HBV, 38% with HCV, 25% with EtOH
- Median GTV 117 cc
- 54% with vascular tumor thrombus
- Dose – 36 Gy (24-54) in 6 fractions

Bujold JCO 2013



1-year Local control 87%

Tumor volume not significant for LC



Bujold JCO 2013

Outcomes After Stereotactic Body Radiotherapy or Radiofrequency Ablation for Hepatocellular Carcinoma

Daniel R. Wahl, Matthew H. Stenmark, Yebin Tao, Erqi L. Pollom, Elaine M. Caoili, Theodore S. Lawrence, Matthew J. Schipper, and Mary Feng

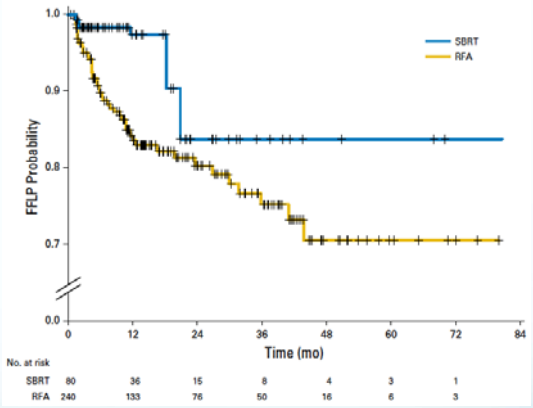
- 224 patients with inoperable HCC treated with:
  - RFA – 161 patients 249 tumors
  - SBRT – 63 patients 83 tumors
- SBRT dose range 27-60 Gy
  - 3 fractions – median 30 Gy
  - 5 fractions – median 50 Gy
- Freedom from local progression
  - Absence of disease progression within or at PTV margin or ablation zone
  - Tumors requiring multiple RFAs for residual disease not counted as failure until after all tumor successfully treated

Wahl JCO 2015

Freedom from local progression

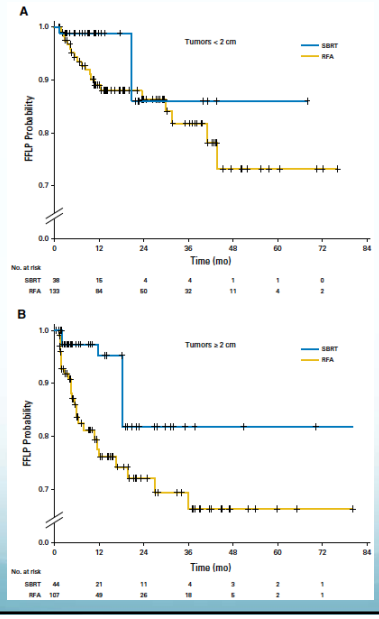
1-year FFLP
RFA – 84%
SBRT – 97%

2-year FFLP
RFA – 80%
SBRT – 84%



Wahl JCO 2015

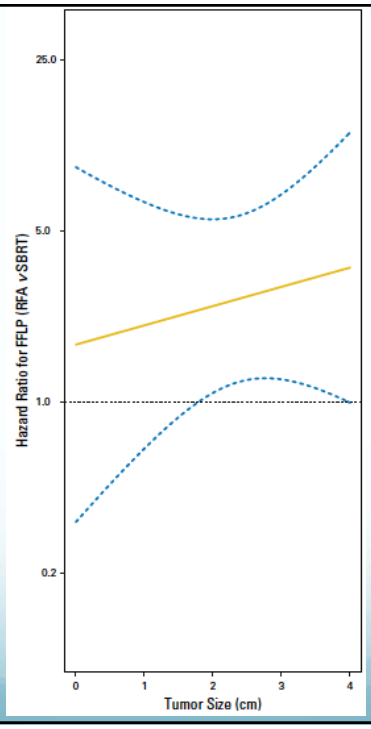
FFLP by size



<2 cm
P=0.15

≥2 cm
P=0.025

Wahl JCO 2015



Favors SBRT

Wahl JCO 2015

RADIATION THERAPY ONCOLOGY GROUP

RTOG 1112

Randomized Phase III Study of Sorafenib versus Stereotactic Body Radiation Therapy followed by Sorafenib in Hepatocellular Carcinoma

SCHEMA

REGISTRATION	**STRATIFY**	Vascular involvement (IVC, main portal vein/right or left main branch portal vein vs. other vascular involvement vs. none) Hepatitis B vs. C vs. other North American site vs. Non-North American site HCC volume/liver volume (<10% vs. 10-40 vs. >40%)	**RANDOMIZE**	**Arm 1** Daily sorafenib **Arm 2** SBRT alone (27.5 Gy – 50 Gy in 5 fractions) Followed by Sorafenib alone daily

https://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?action=openFile&FileID=13150

International HCC SBRT Trial

Residual or recurrent disease following TACE

Randomized
(stratified by tumor size ≤ 3 cm vs > 3 cm)

80 patients → **TACE**

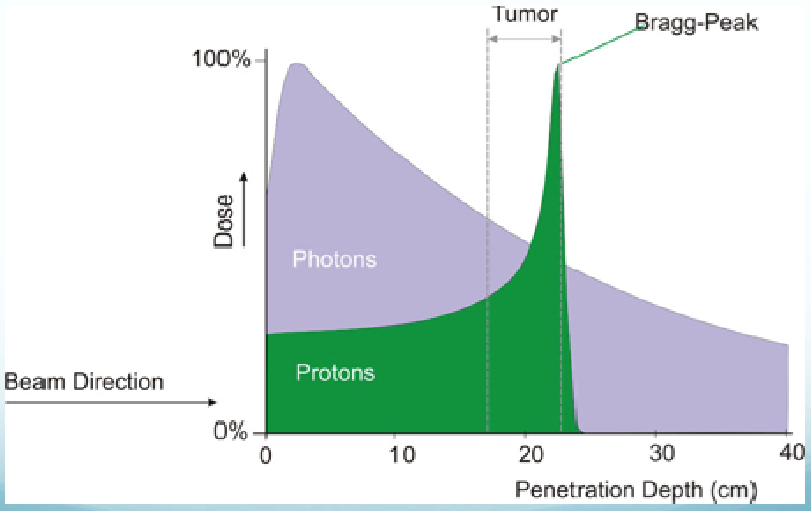
80 patients → **SABR 15 Gy x 3 = 45 Gy**
or 8-10 Gy x 5 = 40-50 Gy with tissue constraints met, see Section 5.3.4.

Crossover between arms allowed at progression
(patients followed on-study after crossover)

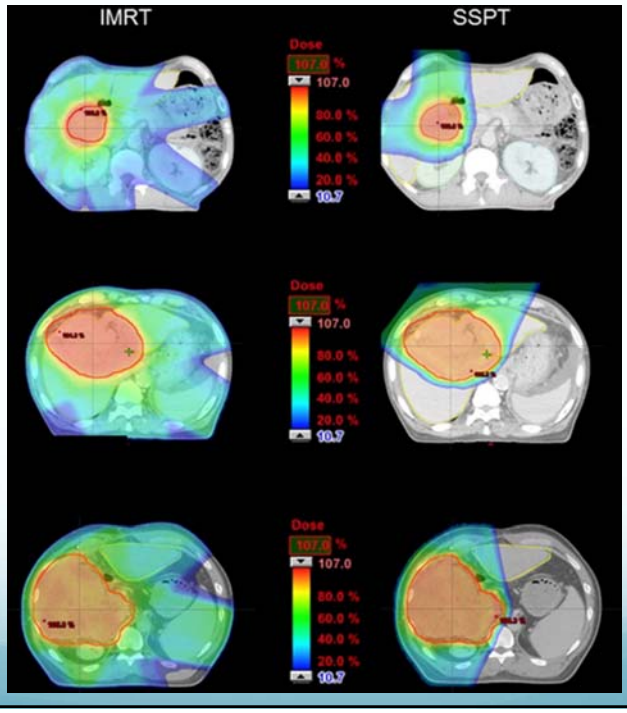
Follow up for 18 months
Follow up for 3 years for survival only

Total sample size: 160

Proton vs photon



Clinics. *Proton Therapy Solutions*. Available at: http://bit.ly/1Ppotod.



Charged Particle Therapy

Author, year	Particle	Dose (GyE)	No. fractions	Survival (1 y)	Survival (5 y)	Toxicity grade ≥3
Bush, 2011	P	63	15	18.4 mo (med)	NA	0%
Komatsu, 2011	P	52-84	4-38	90%*	38%	3%
	C	52.8-76	4-20	87%*	37%	4%
Mizumoto, 2011	P	66-77	10-35	87%	NA	3%
Nakayama, 2011	P	72.6-77	22-35	70%	NA	2%
Sugahara, 2010	P	47.3-89	10-35	64%	NA	0%
Imada, 2010	C	52.8	4	NA	56% (3 y)	39% (all grade 3)
Nakayama, 2009	P	55-77	10-35	90%	NA	2%
Fukumitsu, 2009	P	66	10	90%*	39%	2%
Sugahara, 2009	P	55-77	10-35	45% (2 y)	NA	8%
Mizumoto, 2008	P	72.6	22	57% (2 y)	NA	0%
Hata, 2007	P	60-70	10-35	84%	NA	10%
Hata, 2006	P	63-84	13-27	62% (2 y)	NA	0%
Hata, 2006	P	50-84	10-24	53%	NA	0%
Kawashima, 2005	P	76	20	78%*	62% (3 y)	40% (mostly biochemical†)
Hata, 2005	P	50-72	10-22	88% (2 yr)	NA	0%
Chiba, 2005	P	50-88	10-24	75%	NA	3.1% (grade ≥2)
Kato, 2004	C	49.5-79.5	15	37 mo (med)	NA	26% (1 skin, 10 hematologic)

Klein and Dawson IJROBP 2013

Toxicities

- Classic radiation induced liver disease (RILD)
  - Typically occurs 6 weeks (4-12 weeks) after radiation
  - Clinical – anicteric ascites, hepatomegaly, and 2 X increase in alk phos
  - Pathologic – veno-occlusive disease due to fibrin and collagen deposition within sinusoidal vessels and central veins → vascular congestion → hypoxia/death of centrilobular hepatocytes → hepatic atrophy and dysfunction

Nonclassic RILD

- Non-classic RILD - ≥5 X increase in transaminases – suggesting direct damage to hepatocytes
  - 10/12 patients in Taiwan series had non-classic RILD
  - All patients were carriers of HCV or HBV

Cheng Radiot Oncol 2002

Liver Tolerance

- Child Pugh A cirrhosis appear to have good tolerance to radiation
- Child Pugh B cirrhosis appear to have reduced tolerance to radiation
  - Reduced dose and strict adherence to dose constraints required
- Child Pugh C cirrhosis – little to no data on liver tolerance
  - In general RT should be avoided

Worse tolerance of Child B than Child A

Phase I feasibility trial of stereotactic body radiation therapy for primary hepatocellular carcinoma

- Showed that Child A livers could be safely treated up to 48 Gy at 16 Gy/fraction
- 2/6 patients with Child B developed dose limiting toxicity
- Dose de-escalated to 40 Gy at 8 Gy/fraction

Cardenes et al, Clin Tranl Oncol 2010

Treatment variables related to liver toxicity in patients with hepatocellular carcinoma, Child-Pugh class A and B enrolled in a phase 1-2 trial of stereotactic body radiation therapy

No association of liver dosimetry with toxicity in Child A patients

Higher liver dosimetry seen in patients with toxicity in Child B patients

Table 3 Dosimetry data by hepatic toxicity in Child-Pugh class B patients

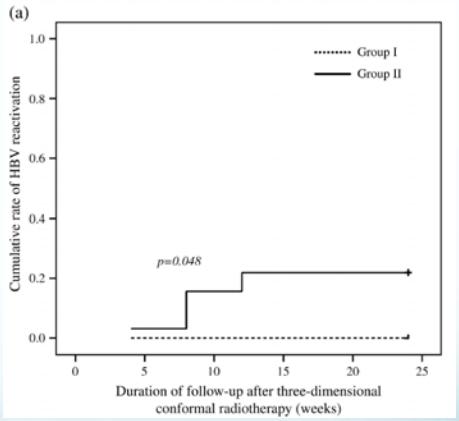
Maximal dose to normal volume in CPC-B patients	Normal volume receiving dose without hepatic toxicity	Normal volume receiving dose with grade III/IV hepatic toxicity	*P* value
<15 Gy	1053.1 mL	1515.9 mL	.0396
<12.5 Gy	946.1 mL	1432.0 mL	.0254
<10 Gy	797.8 mL	1293.0 mL	.0132
<7.5 Gy	625.9 mL	1149.7 mL	.0041
<5 Gy	480.8 mL	1024.1 mL	.0015
<2.5 Gy	304.9 mL	810.8 mL	.0011

CPC-B, Child-Pugh class B.

Lasley PRO 2015

Caution: *HBV reactivation*

- Reported after conventional RT for HCC
- Consider in differential diagnosis of radiation-induced liver disease in high risk pt
- Antiviral therapy likely reduces risk
  - Figure at right:
    - Group I antiviral therapy
    - Group II none

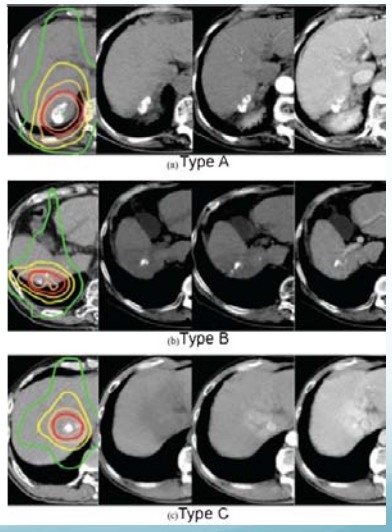


Kim et al. IJROBP 69(3): 813–819, 2007
Center for Liver Cancer, South Korea

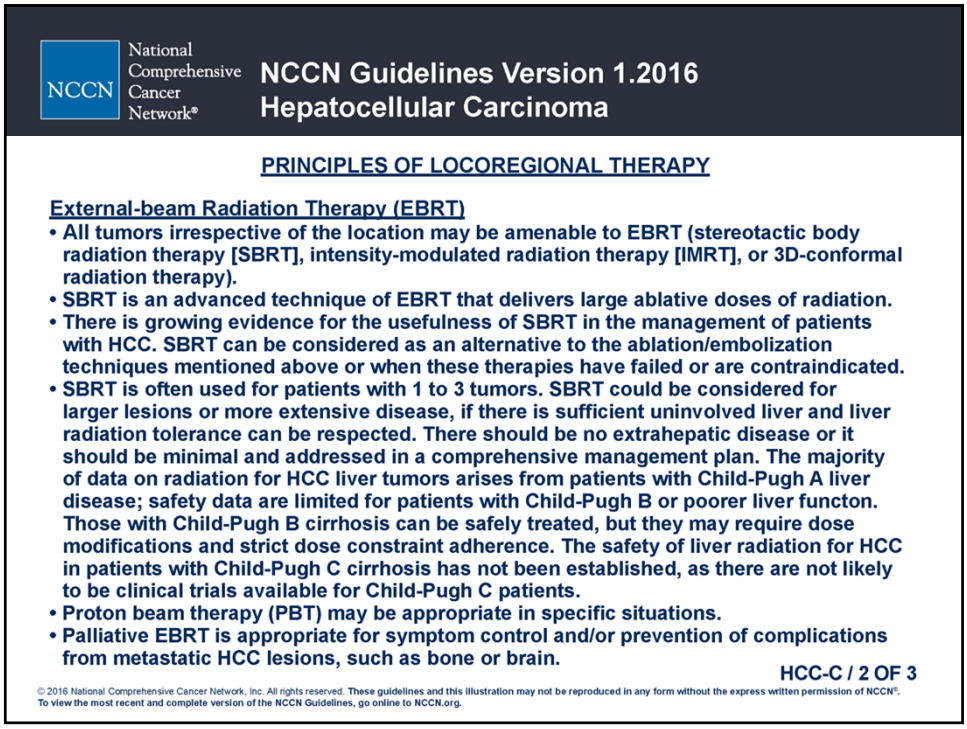
Courtesy of B. Kavanagh

Don't confuse post-radiation change with recurrence

	Pre	Art	PV
Type A	Iso	Iso	Iso
Type B	Low	Iso	Iso
Type C	Low	Iso or High	High



Sanuki-Fujimoto Br J Rad 2010



Conclusions

- EBRT is an important and effective treatment option for HCC
- Improvements in technology have allowed safe delivery of ablative doses of radiation with excellent control rates
- Further studies and ideally randomized trials with other liver-directed therapies are needed in the overall treatment algorithm for HCC
- Need better understanding of liver tolerance to optimize dose fractionation