Recent Advances in Radiotherapy for the treatment of liver cancer

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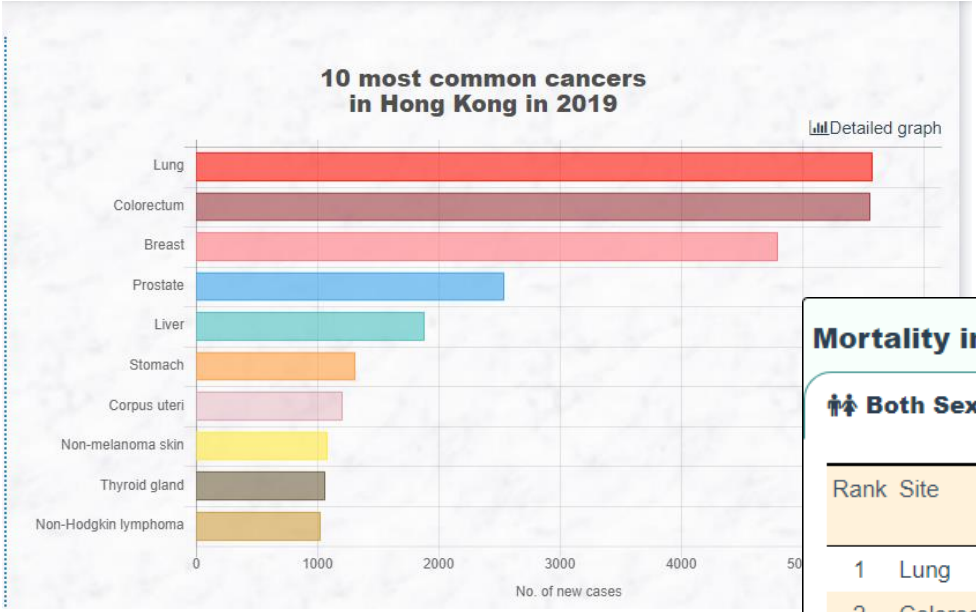
Outline

- Overview of Liver cancer
  - Prevalence
  - Risk factors
  - Symptoms
  - Investigation
  - Overview of treatment options
- SBRT for Hepatocellular carcinoma
  - What is radiotherapy and SBRT?
  - The myths
  - Advances in technology
  - Published Evidence
  - cases
  - Summary

Liver cancer --prevalence

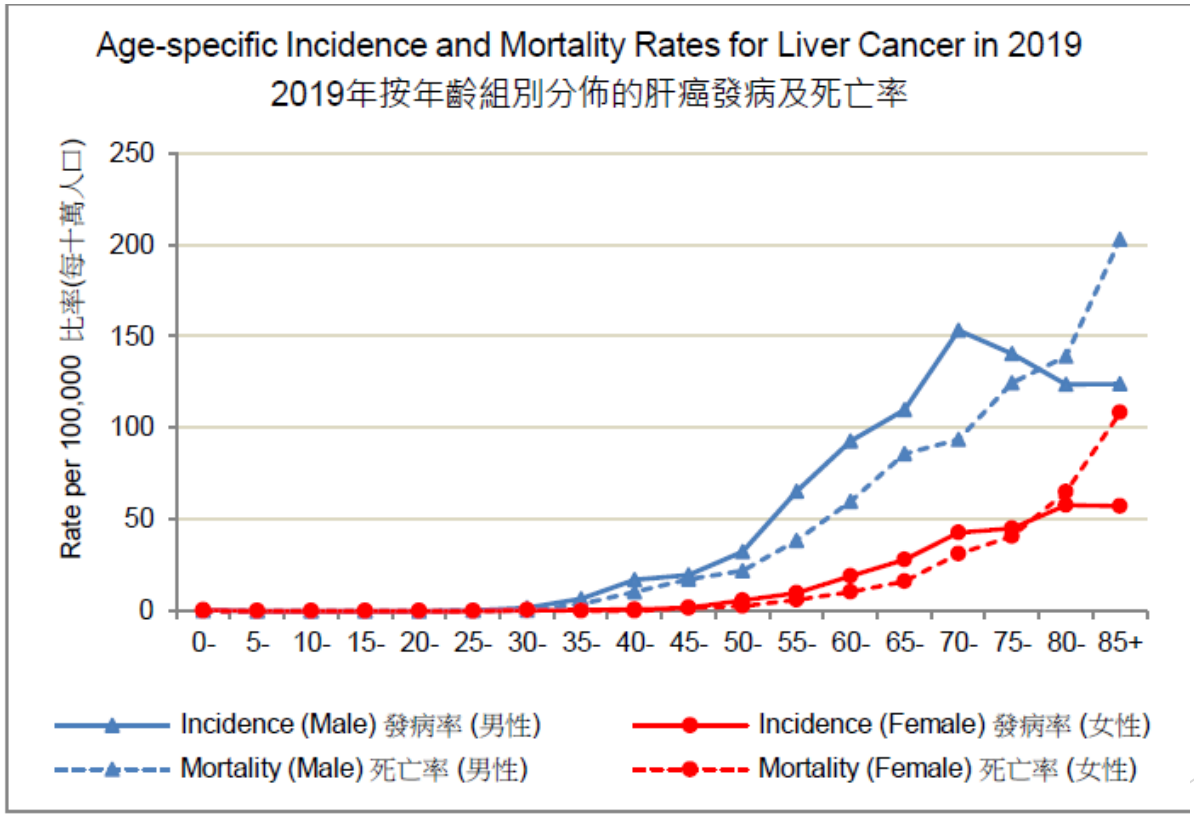


Mortality in 2019 - Both Sexes

Both Sexes | Male | Female

Rank	Site	No.	Rel. Freq.	Crude rate*
1	Lung	4,033	27.1%	53.7
2	Colorectum	2,174	14.6%	29.0
3	Liver	1,530	10.3%	20.4
4	Breast	859	5.8%	11.4
5	Pancreas	740	5.0%	9.9
6	Stomach	696	4.7%	9.3
7	Prostate	445	3.0%	13.0
8	Non-Hodgkin lymphoma	403	2.7%	5.4
9	Oesophagus	320	2.2%	4.3
10	Leukaemia	298	2.0%	4.0
	All Sites (Include other sites not listed above)	14,871	100.0%	198.1

Liver cancer --prevalence

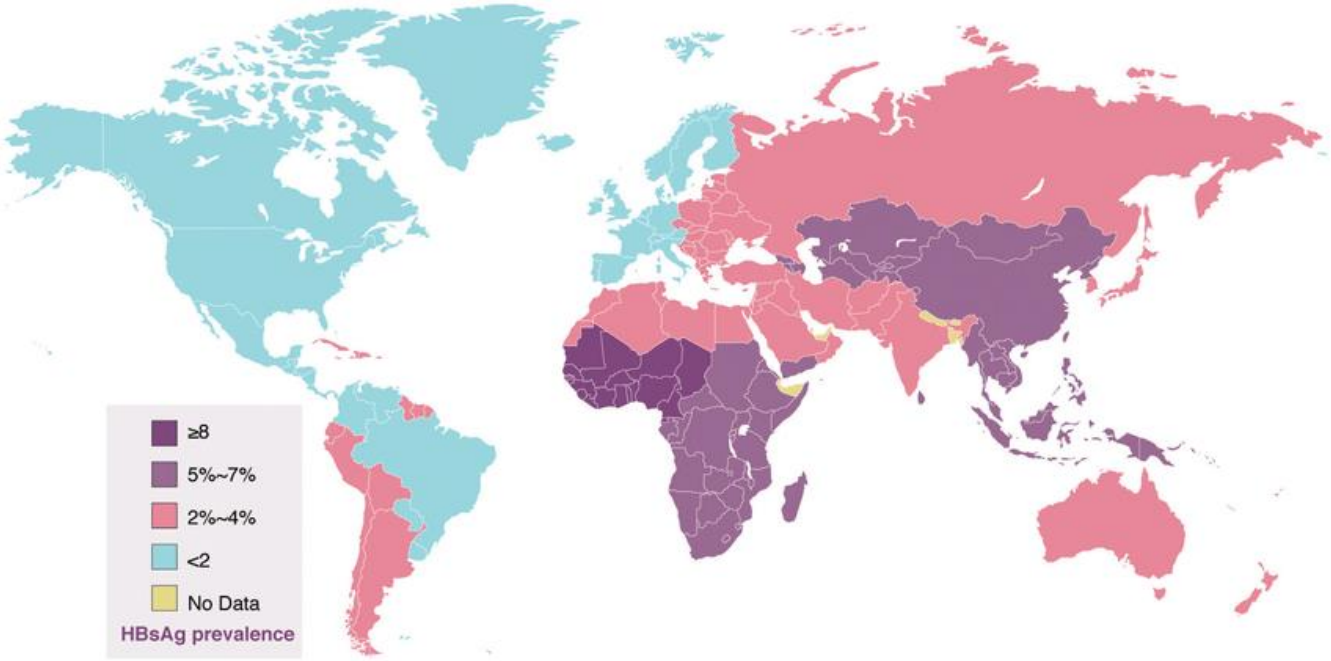


Hong Kong Cancer Registry

Liver cancer—Risk factors

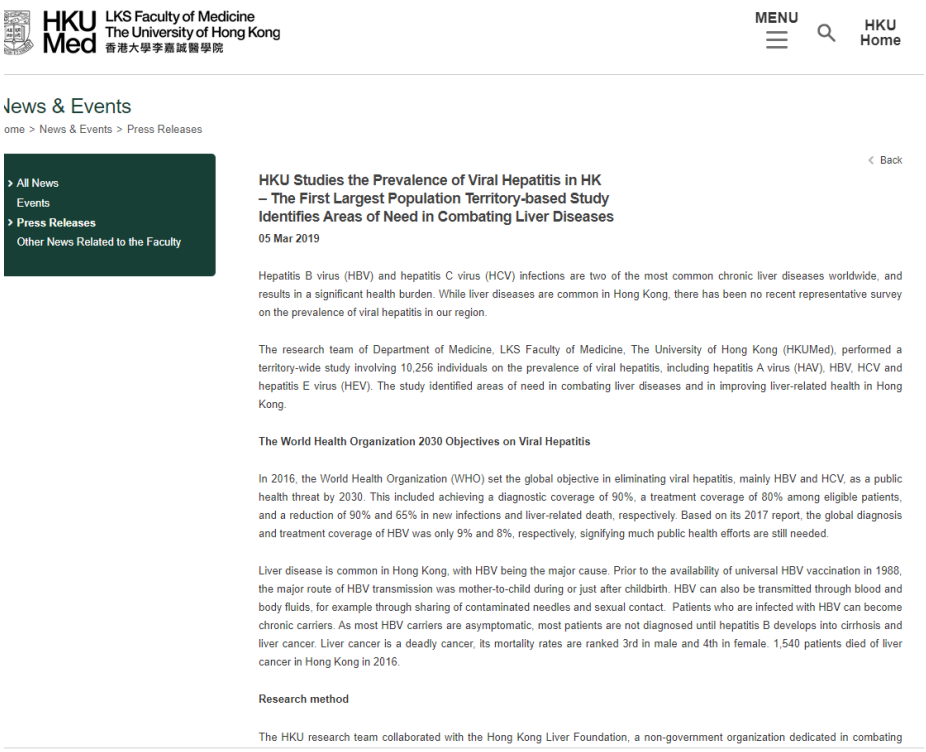
- Cirrhosis
  - Hepatitis B :3.2 (with cirrhosis) versus 0.1 cases (without cirrhosis) per 100 person-years
  - Hepatitis C cirrhosis :risk of developing HCC once cirrhosis has developed have ranged from 1 to 4 percent per year
  - Alcoholic cirrhosis: 2.9 cases per 100 patient-years
  - Environmental toxin: Aflatoxin B1 , Betel nut chewing
  - nonalcoholic fatty liver disease NASH cirrhosis: 1 per 100 person-years

Liver cancer --Risk factors Hepatitis B



CDC 2010

Liver cancer --Risk factors Hepatitis B



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HKU Studies the Prevalence of Viral Hepatitis in HK – The First Largest Population Territory-based Study Identifies Areas of Need in Combating Liver Diseases

05 Mar 2019

Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are two of the most common chronic liver diseases worldwide, and results in a significant health burden. While liver diseases are common in Hong Kong, there has been no recent representative survey on the prevalence of viral hepatitis in our region.

The research team of Department of Medicine, LKS Faculty of Medicine, The University of Hong Kong (HKUMed), performed a territory-wide study involving 10,256 individuals on the prevalence of viral hepatitis, including hepatitis A virus (HAV), HBV, HCV and hepatitis E virus (HEV). The study identified areas of need in combating liver diseases and in improving liver-related health in Hong Kong.

The World Health Organization 2030 Objectives on Viral Hepatitis

In 2016, the World Health Organization (WHO) set the global objective in eliminating viral hepatitis, mainly HBV and HCV, as a public health threat by 2030. This included achieving a diagnostic coverage of 90%, a treatment coverage of 80% among eligible patients, and a reduction of 90% and 65% in new infections and liver-related death, respectively. Based on its 2017 report, the global diagnosis and treatment coverage of HBV was only 9% and 8%, respectively, signifying much public health efforts are still needed.

Liver disease is common in Hong Kong, with HBV being the major cause. Prior to the availability of universal HBV vaccination in 1988, the major route of HBV transmission was mother-to-child during or just after childbirth. HBV can also be transmitted through blood and body fluids, for example through sharing of contaminated needles and sexual contact. Patients who are infected with HBV can become chronic carriers. As most HBV carriers are asymptomatic, most patients are not diagnosed until hepatitis B develops into cirrhosis and liver cancer. Liver cancer is a deadly cancer, its mortality rates are ranked 3rd in male and 4th in female. 1,540 patients died of liver cancer in Hong Kong in 2016.

Research method

The HKU research team collaborated with the Hong Kong Liver Foundation, a non-government organization dedicated in combating

HKU study: Hepatitis B infection prevalence in HK 7.8%

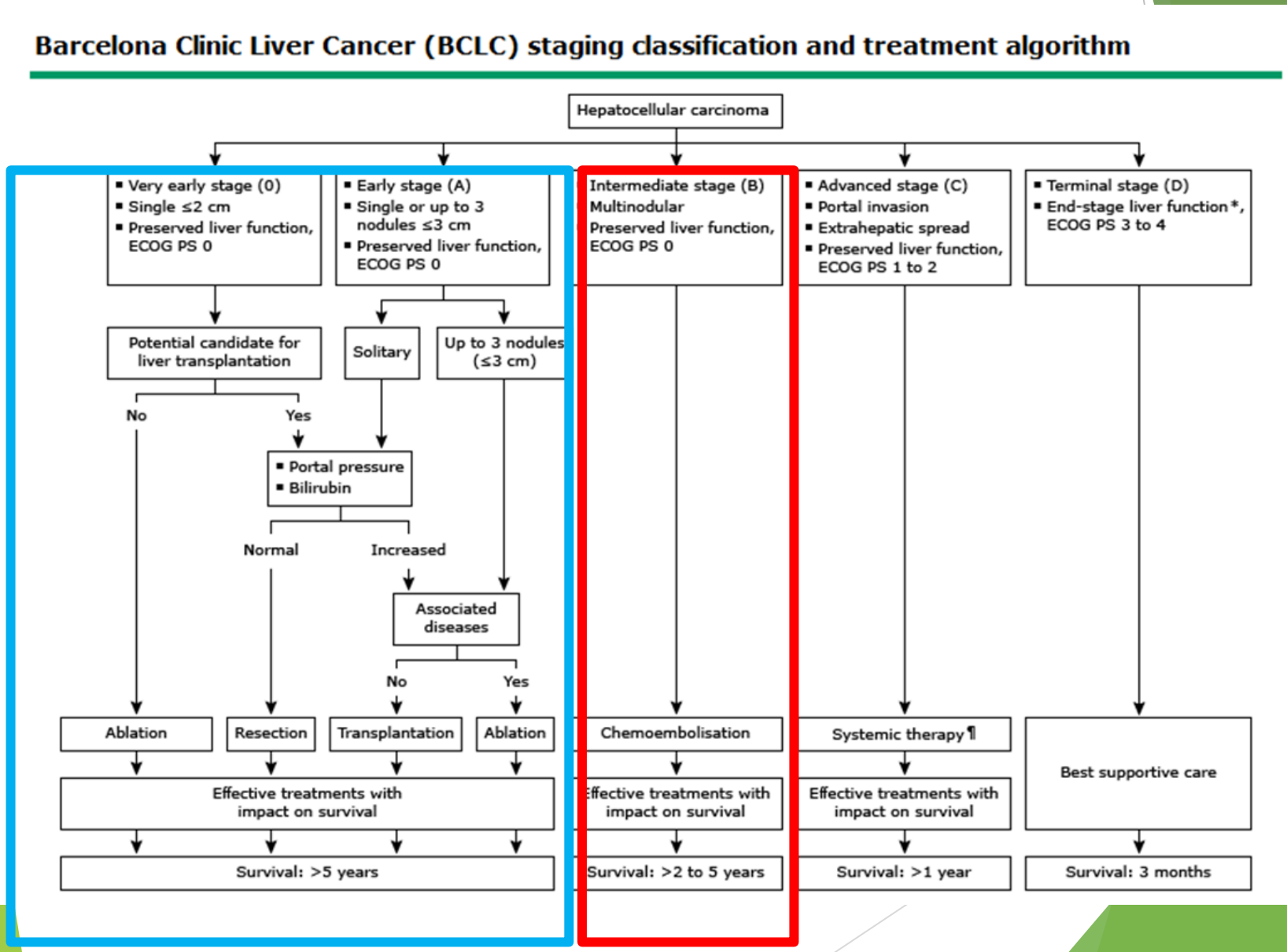
Liver cancer-- symptoms

- Local symptoms
- Symptoms of liver decompensation
  - Ascites
  - Ankle edema
  - Jaundice
  - hypoglycemia
- Symptoms of distant metastasis
  - Bone pain
  - Pleural effusion

Liver cancer--investigation

- Triphasic CT
- C-Acetate PET
- Blood x AFP, LFT
- Biopsy only indicated in cases without preexisting risk factors and atypical enhancement features

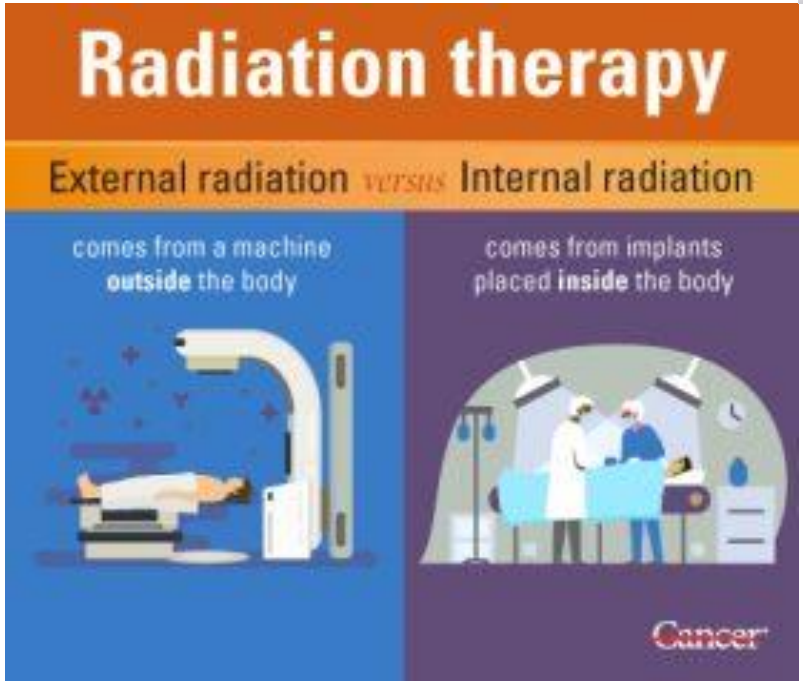
Liver cancer—treatment option by stage



What is radiotherapy?

Basic radiobiology

LINAC
COBALT 60
Gamma Knife
Cyber Knife
Carbon ion therapy
Superficial Xray
Electron therapy
Tomotherapy
Proton therapy



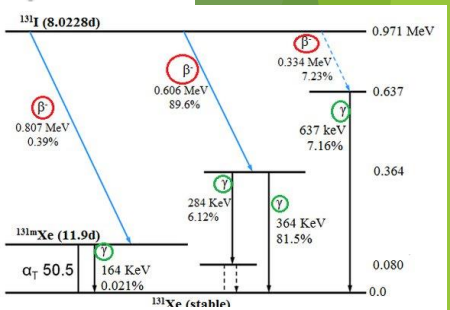
- Brachytherapy: Afterloading technique
- Iodine 131 ingestion
- Radioembolization (Y90)

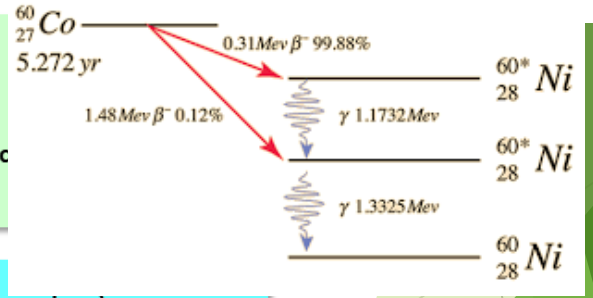
Basic radiobiology

Isotope	Emission	Mean energy (MeV)	Half-life (days)
Iodine-125	γ	0.028	60
Iridium-192	γ	0.38	74
Phosphorus-32	β	0.69	14
Rhenium-186	β	0.36	4
Yttrium-90	β	0.93	3

Radiation Types of Radiation

- **Ionizing radiation**
  - Particle beams
    - Charged-particle beams (directly ionizing radiation)
      - α-particles (helium nuclei ejected from a nucleus)
      - β-particles (electrons ejected from a nucleus)
      - Proton beams, deuteron beams, triton beams, heavy-ion beams
      - Charged meson beams
      - Fission fragments, etc.
    - Uncharged particle beams (indirectly ionizing radiation)
      - Uncharged meson beams
      - Neutrino
      - Neutron beams, etc. (produc accelerators, etc.)
  - Electromagnetic waves (indirectly ionizing radiation)
    - X-rays (generated outside a nucleus)
    - γ-rays (emitted from a nucleus)
- Nonionizing radiation — Electric waves, microwaves, infrared rays, visible rays, ultraviolet rays, etc.

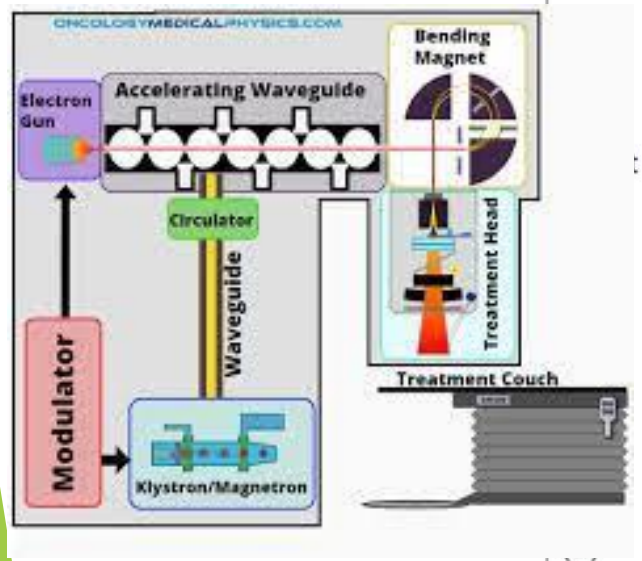


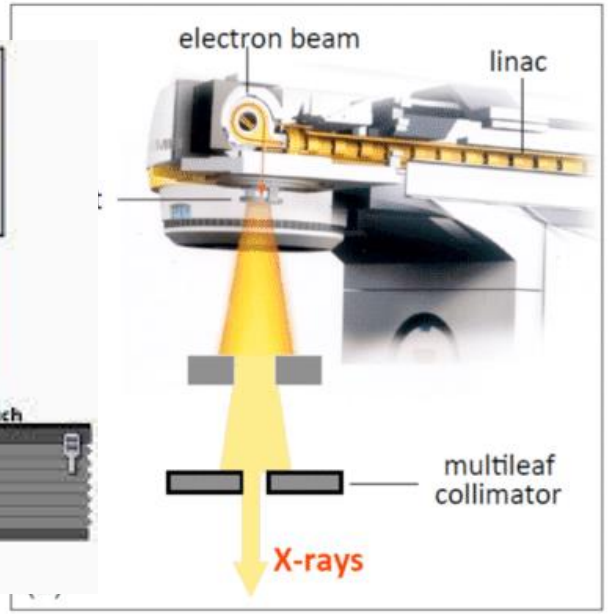


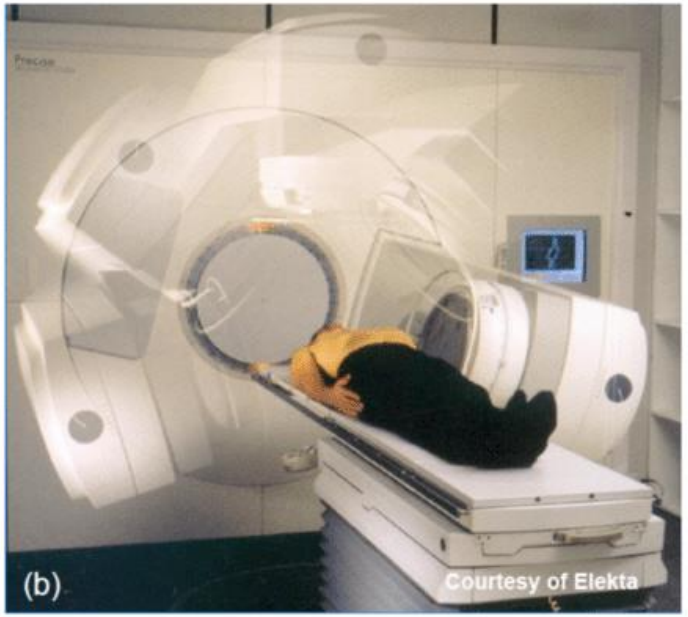
While radiation includes ionizing radiation and nonionizing radiation, radiation usually means ionizing radiation.

Partially revised "Ionizing Radiation" in the Encyclopedia for Public Acceptance of Atomic Energy Accessible on the Internet, ATOMICA

Basic radiobiology—inside a LINAC



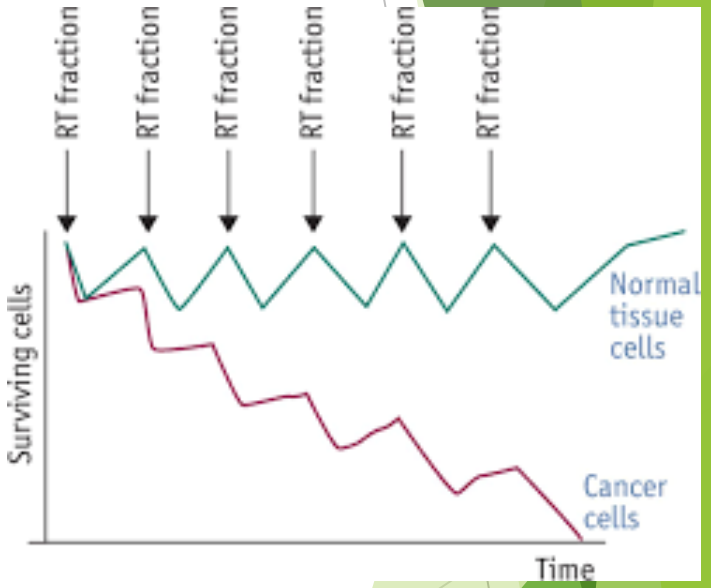




Basic radiobiology—scientific basis

- **Gray (Gy)** :SI unit of radiation dose, expressed as absorbed energy per unit mass of tissue.
- 1 Gy = 1 Joule/kilogram = 100 rad.
- Gray can be used for any type of radiation (e.g., alpha, beta, neutron, gamma)

Radiobiology—behaviour of cancer cells and normal tissue



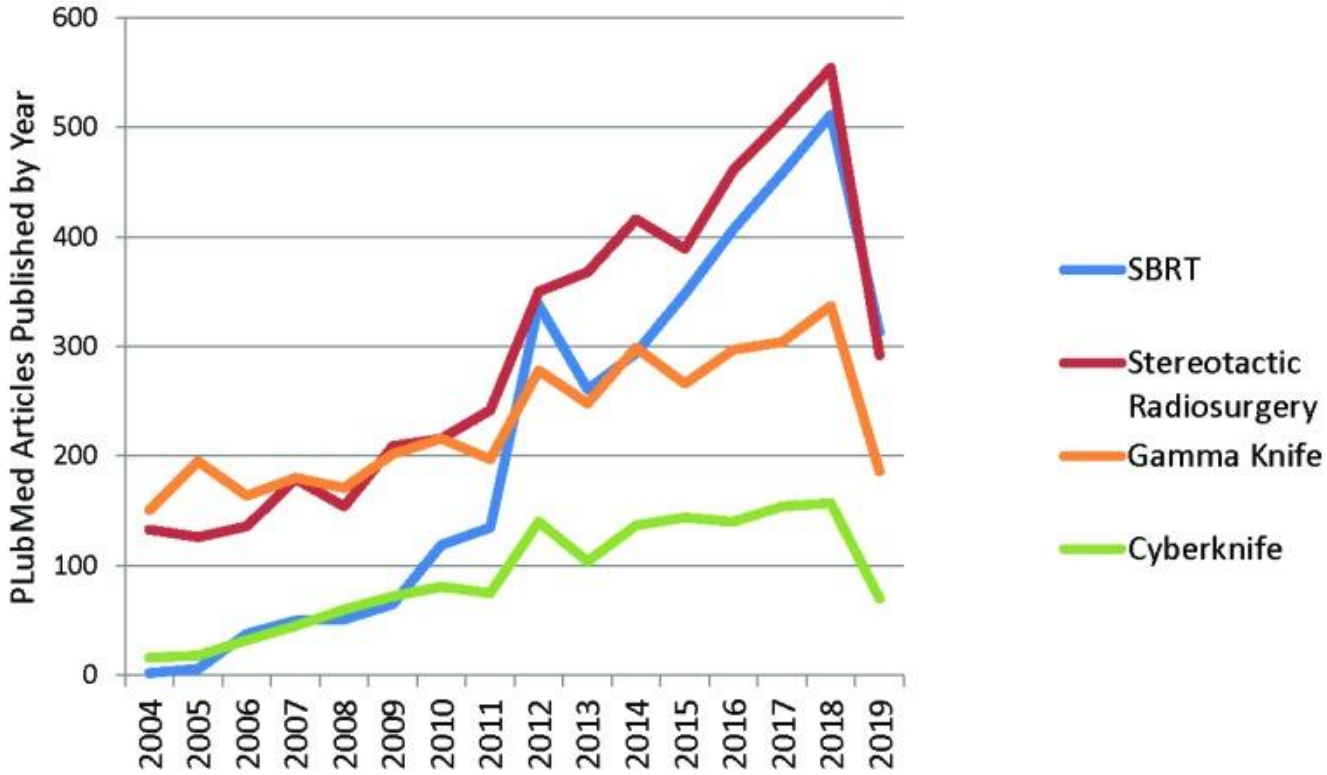
What is Stereotactic body radiation therapy (SBRT)?

SBRT ?

stereotactic radiotherapy?

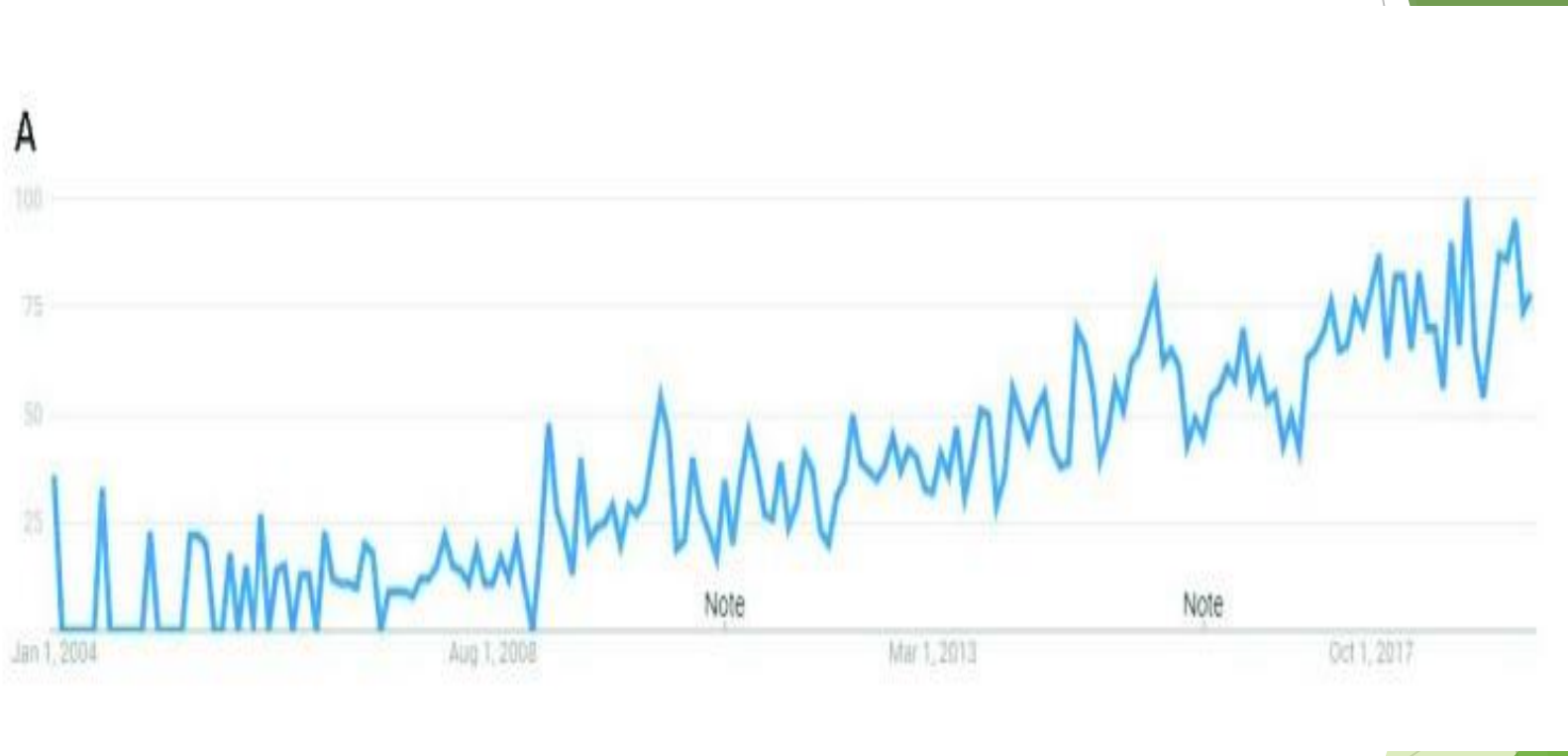
fractionated stereotactic radiosurgery ?

PubMed articles published by year



Malouff TD, Seneviratne D, Stross WC, Ko S, Tzou K, Trifiletti DM, Vallow LA. Public interest in stereotactic body radiation therapy (SBRT) and stereotactic radiosurgery (SRS) in the United States. J Radiosurg SBRT. 2020;6(4):311-315. PMID: 32185091; PMCID: PMC7065901.

Google Search for ‘SBRT’



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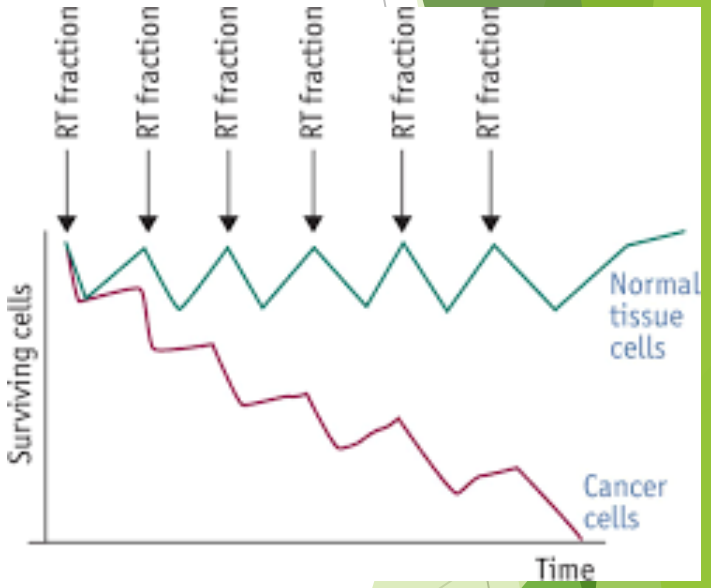
What is SBRT: Radiobiology

<2Gy/Fr
Hyperfractionation

2Gy/Fr

>2Gy/Fr
Hypofractionation

Radiobiology—behaviour of cancer cells and normal tissue

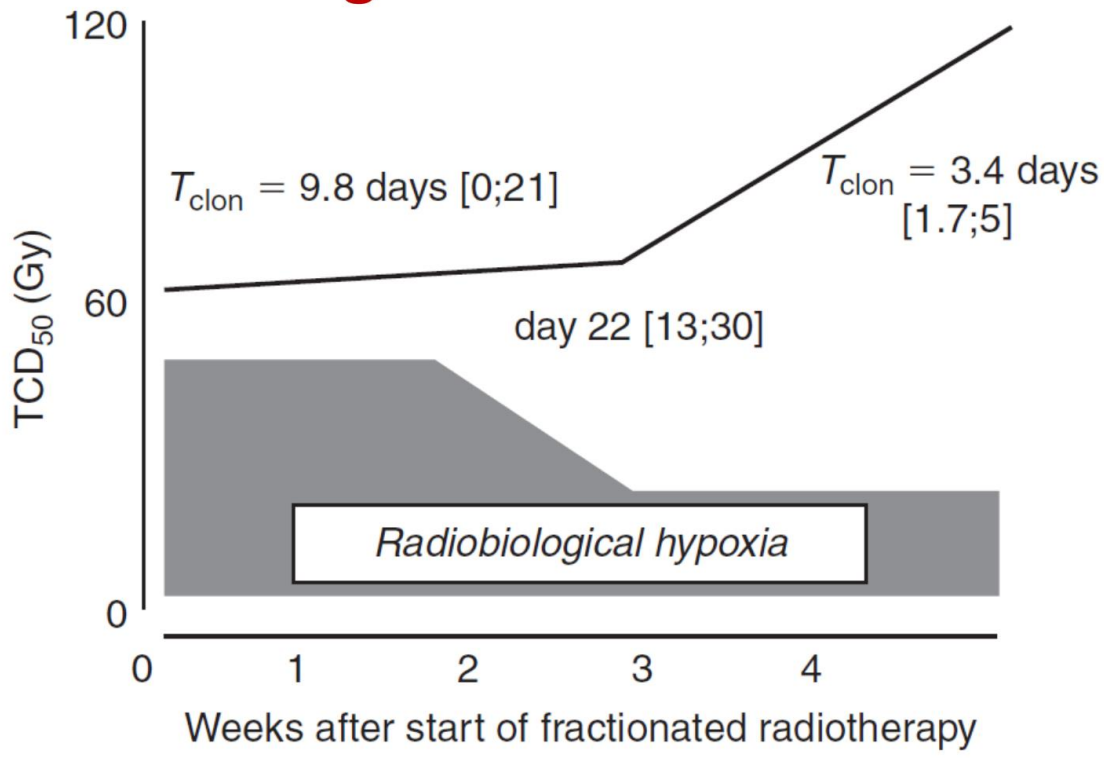


What is SBRT? The 5Rs that determines effect of RT

- Repair
- Reoxygenation: Fractional allows for reoxygenation of more hypoxic cells and make them more susceptiable to radiation
- Reassortment : Fractionation allows for cells to proceed to more radiosensitive phase in the cell cycle
- **Repopulation: prolonged waiting time between fractions results in regrowth of tumour cells from sublethal damage**
- Radiosensitivity(intrinsic) of tumour

Radiobiology –Time factor

Biphasic course of clonogen **repopulation** during fractionated RT



Petersen *et al*. IJROBP (2001) 51: 483–93.

What is SBRT: Are they equal?

2Gy x 25Fractions = 10Gy x 5 Fractions?

Conventional dose , adjuvant RT for breast cancer

SBRT dose, Ablative RT for liver cancer

What is SBRT?
Definition from ACR and ASTRO

an external beam radiation therapy method

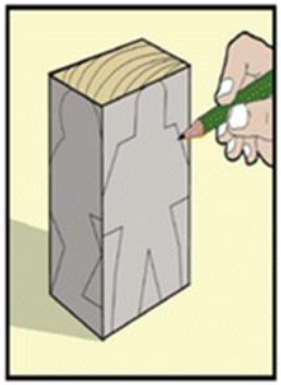
very precisely deliver a high dose of radiation

to an extracranial target within the body

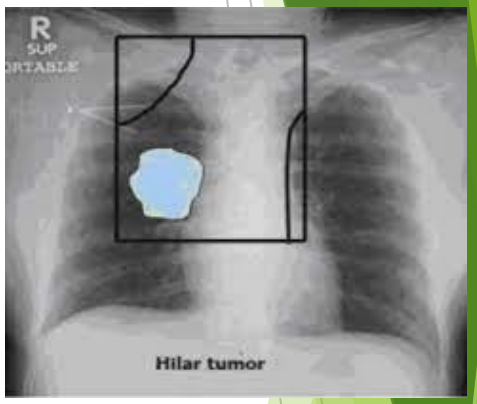
using either a single dose or a small number of fractions.

What makes SBRT possible? Improvement in conformality

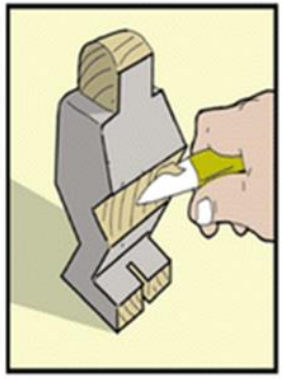
Conventional



2D – Conformal

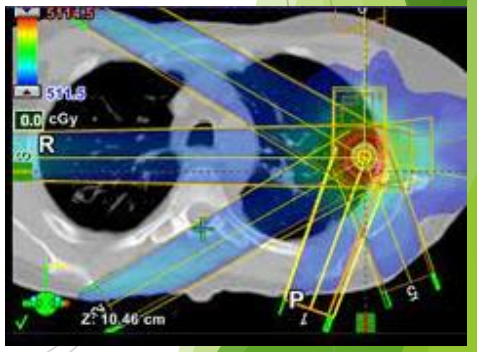


3D – Conformal

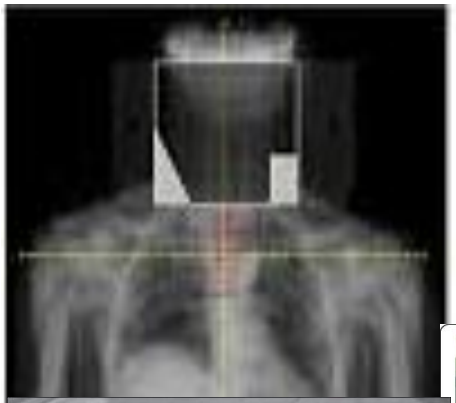


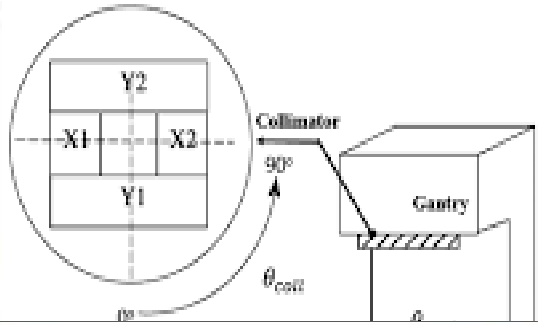
IMRT

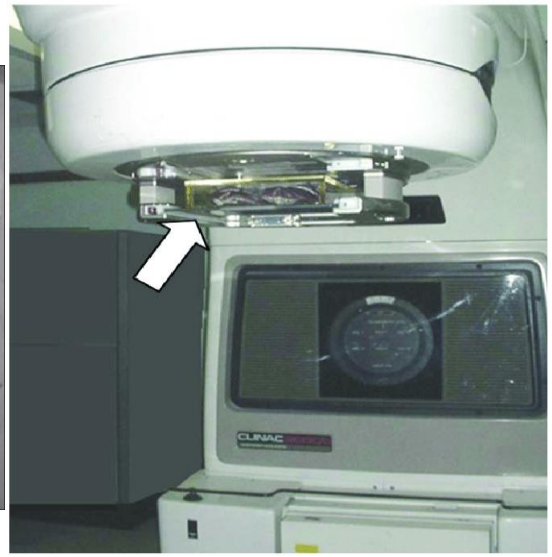
Intensity modulated radiotherapy

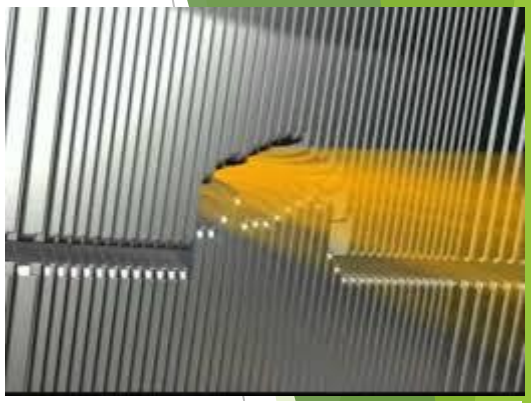


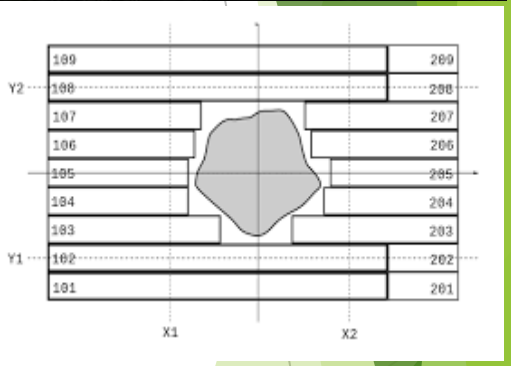
What makes SBRT possible? Improvement in conformality



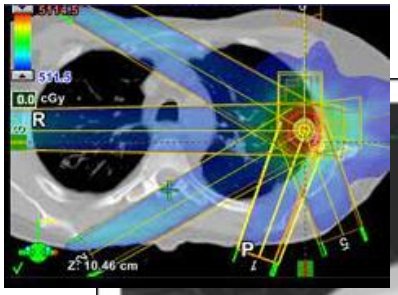


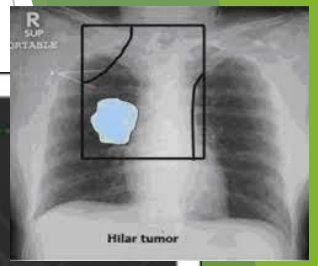






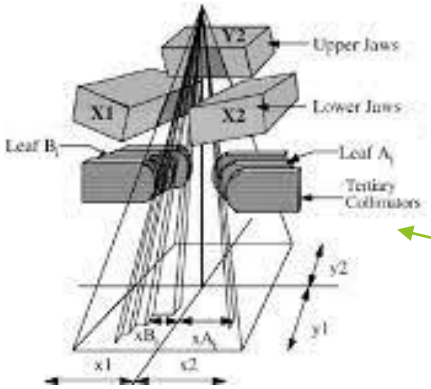
What makes SBRT possible? Improvement in conformality

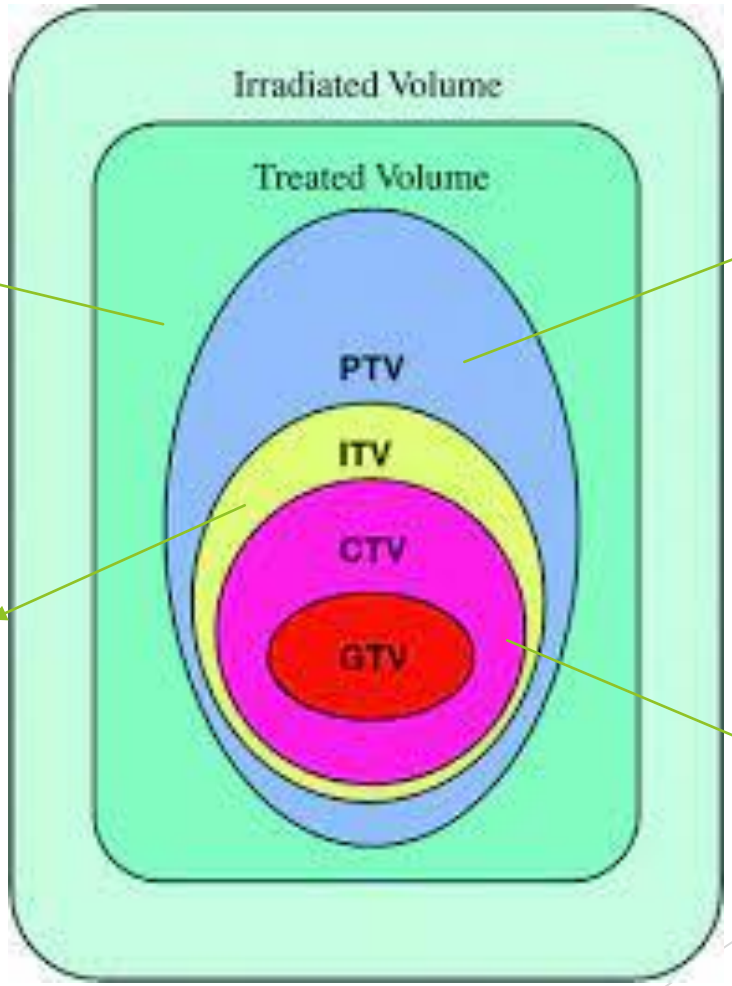


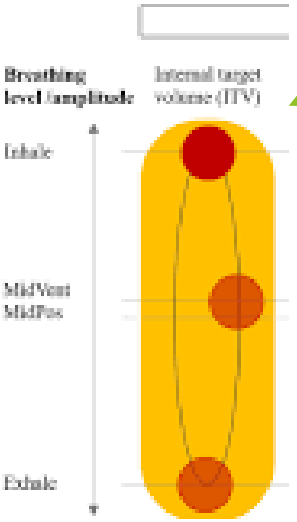


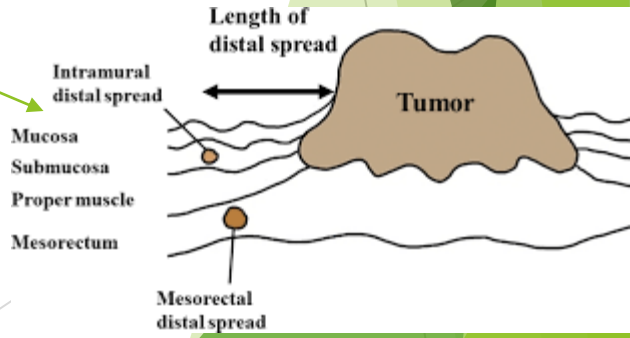
Timmerman RD, Herman J, Cho LC. Emergence of stereotactic body radiation therapy and its impact on current and future clinical practice. J Clin Oncol. 2014;32(26):2847-2854. doi:10.1200/JCO.2014.55.4675

What makes SBRT possible? Reduction of margins





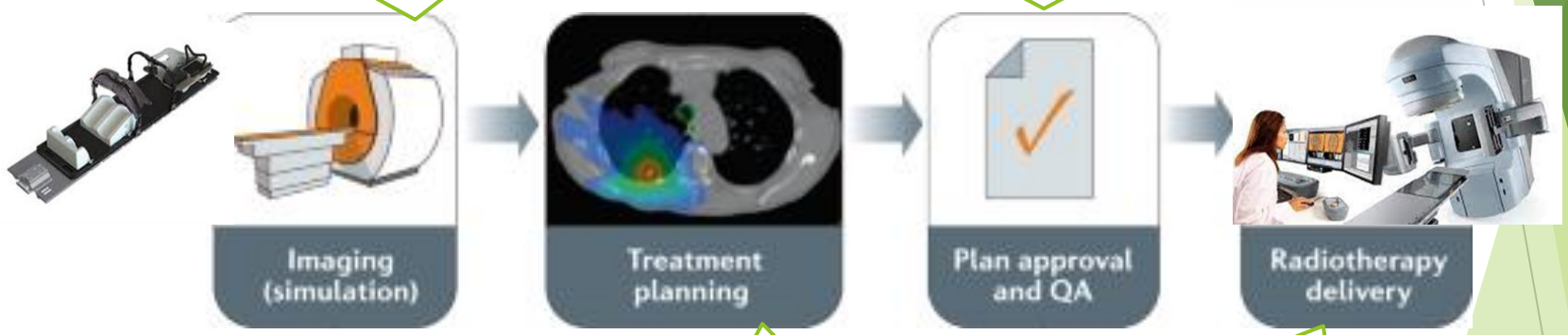




What makes SBRT possible? Reduction of margins

1)Thin cut planning CT
2)Respiratory motion control
3) Better immobolization

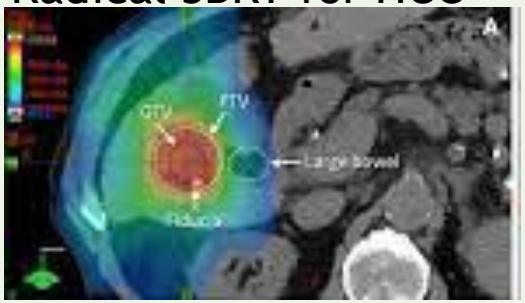
Additional Quality Assurance procedures by physicists



1)Treatment planning with IMRT
2) Co-registration with MRI/PET

1) IGRT: Verification using cone beam CT
2) RT delivered by IMRT/VMAT
3) Respiratory motion control
4) Better immobolization

What is SBRT? The applications

	Normal fractionation (1.8-2Gy/Fr)	SBRT
Usage	RT to prophylactic volumes (at risk but without Gross tumour volume) to reduce recurrence	focused volume consisting of gross tumour only
Example	Adjuvant RT for breast 	Radical SBRT for HCC 
efficacy	Adjuvant RT for post BCT breast cancer :10-year risk of any first recurrence : 35 %(BCT alone) Vs 19% (+adj RT)	SBRT HCC :local tumor control rates 2-3 years following SBRT : 68 to 95% [2]

1 Senthi S, Lagerwaard FJ, Haasbeek CJ, Slotman BJ, Senan S. Patterns of disease recurrence after stereotactic ablative radiotherapy for early stage non-small-cell lung cancer: a retrospective analysis. Lancet Oncol. 2012 Aug;13(8):802-9. doi: 10.1016/S1470-2045(12)70242-5. Epub 2012 Jun 22. PMID: 22727222

2Ohri N, Tomé WA, Méndez Romero A, Miften M, Ten Haken RK, Dawson LA, Grimm J, Yorke E, Jackson A. Local Control After Stereotactic Body Radiation Therapy for Liver Tumors. Int J Radiat Oncol Biol Phys. 2021 May 1;110(1):188-195. doi: 10.1016/j.ijrobp.2017.12.288. Epub 2018 Jan 6. PMID: 29395629; PMCID: PMC6102100.

What is SBRT: Are they equal?

	2Gy x 25Fr	10Gy x 5Fr
	Conventional fractionation (adjuvant radiotherapy for breast cancer)	SBRT dose fractionation (Ablative RT for lung /liver cancer)
BED $_{10}$	60Gy	100Gy
EQD2	Early or Late :50Gy	Early (tumour) :83.3 Gy Late :150 Gy

$$\mathrm{BED} = nd\left[1 + \frac{\mathrm{d}}{(\alpha/\beta}\right]$$

$$EQD_2 = \frac{BED}{1 + \frac{2}{\alpha/\beta}}$$

SBRT for HepatoCellular Carcinoma

Myths on Radiotherapy for HCC

- not a ‘radiosensitive’ tumor
- radiotherapy is too ‘toxic’ for the liver
  - RILD is seen in 5–10% of patients treated with 30–35 Gy to the whole liver.
- Impossible to irradiate a moving organ

Myths on Radiotherapy for HCC

Table 1. Hepatocellular carcinoma radiosensitivity described in terms of SF2 and LQ parameters.

Cell Line	Parameter	Number of Cell Lines	Mean	Median	Min.	Max.	SD	References
All tumors excluding HCC	SF_2	134	0.37	0.35	0.001	0.86	0.20	[8]
HCC (primary cultured cells)	SF_2	29	0.41		0.28	0.78	0.05	[7,9]
HepG2, Hep3b	SF2	2			0.34	0.67		[5]
	α/β (Gy)				3.1	7.4		
	α (Gy^{-1})				0.118	0.413		
	β (Gy^{-2})				0.038	0.056		
HepG2, Hep3b	α (Gy^{-1})	2			0.185	0.249		[6]
	β (Gy^{-2})				0.124	0.172		
SMMC-7721, SK-HEP-1	α /β (Gy)	2			1.57	6.64		[8]
	α (Gy^{-1})				0.09	0.37		
	β (Gy^{-2})				0.05	0.06		

HCC, hepatocellular carcinoma; SD, standard deviation.

SBRT for HCC—myths
Too toxic

Moving Target

- HCC moving along with respiratory motion of liver (increased superior-inferior irradiated volume to encompress whole track of tumour)

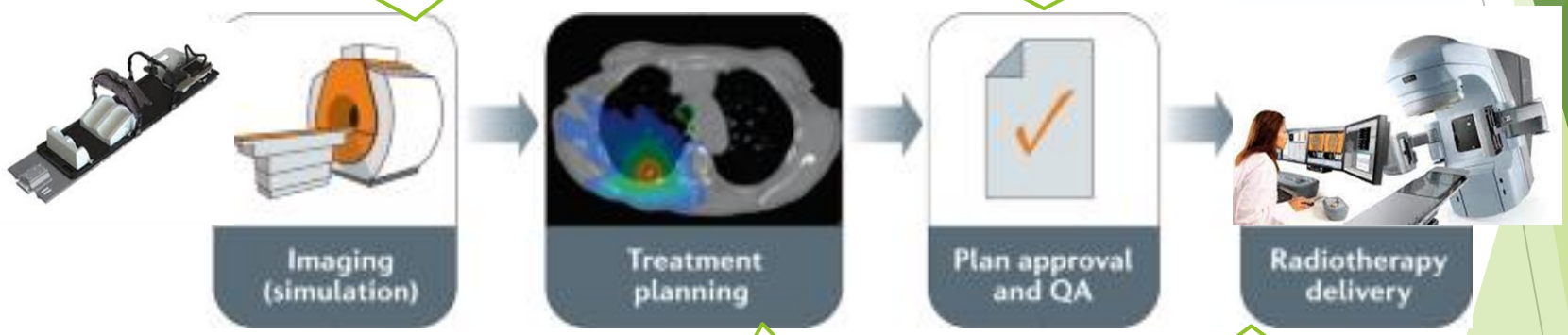
Surrounding Organ At Risk :

- Liver (often cirrhotic)
- Stomach
- Small bowel
- Spinal cord

What is SBRT?

1)Thin cut planning CT
2)Respiratory motion control
3) Better immobolization

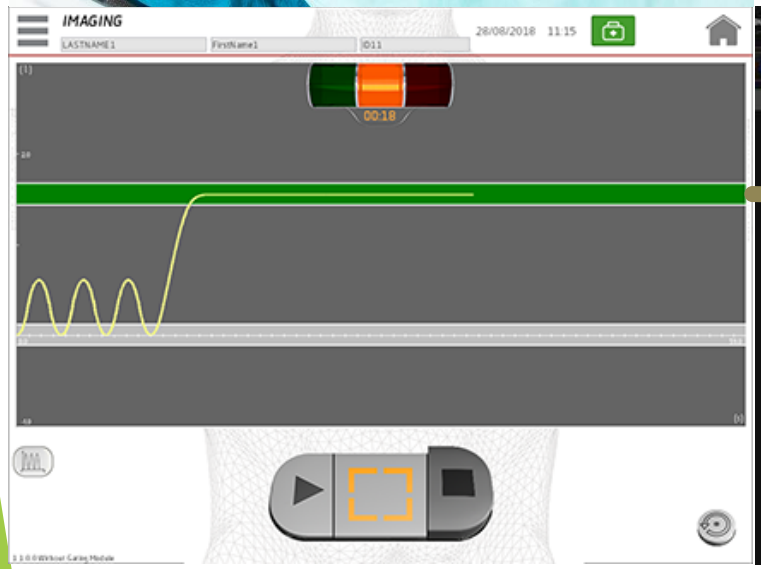
Additional Quality Assurance procedures by physicists

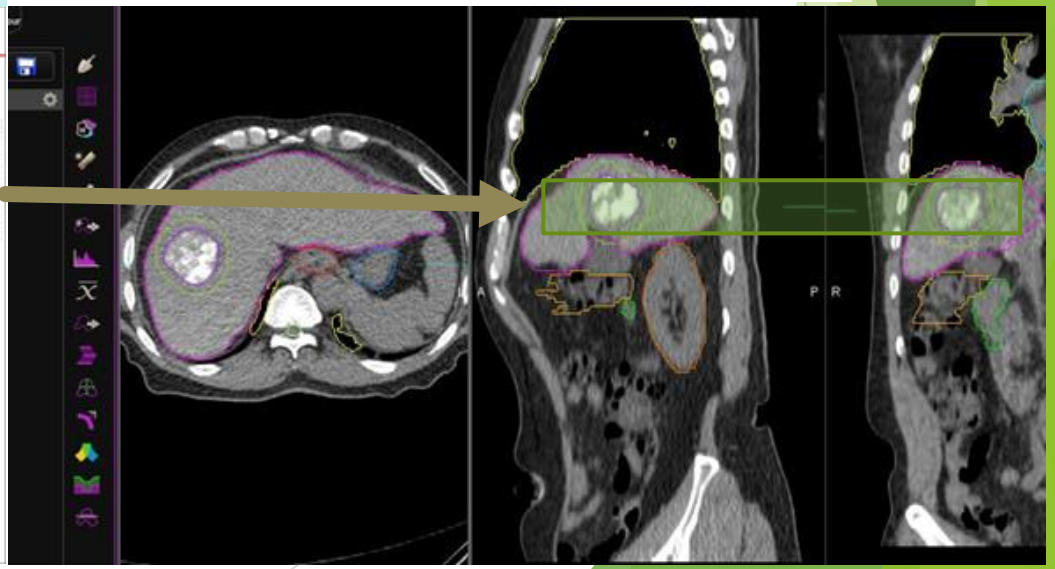


1)Treatment planning with IMRT
2) Co-registration with MRI/PET

1) IGRT: Verification using cone beam CT
2) RT delivered by IMRT/VMAT
3) Respiratory motion control
4) Better immobolization

SBRT for HCC—myths
Too toxic (respiratory motion

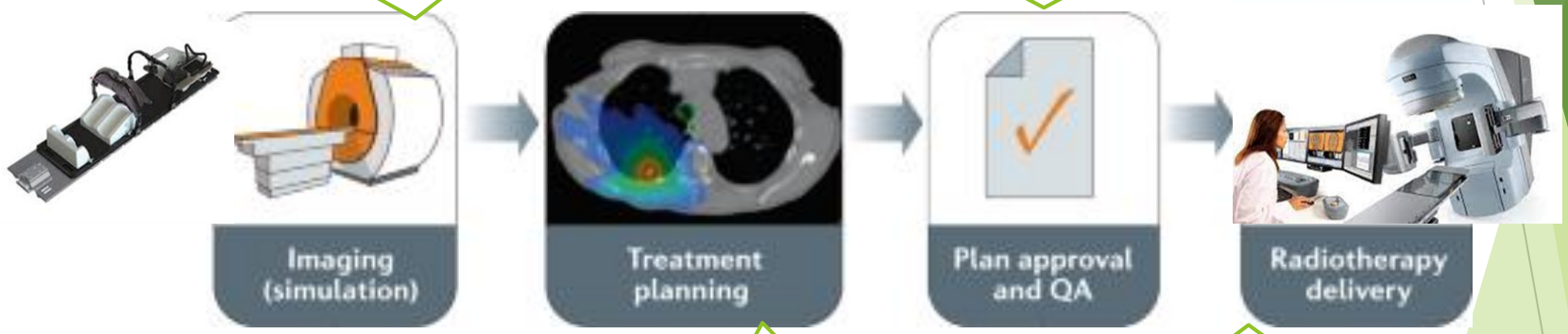




What is SBRT?

1)Thin cut planning CT
2)Respiratory motion control
3) Better immobolization

Additional Quality Assurance procedures by physicists



1)Treatment planning with IMRT
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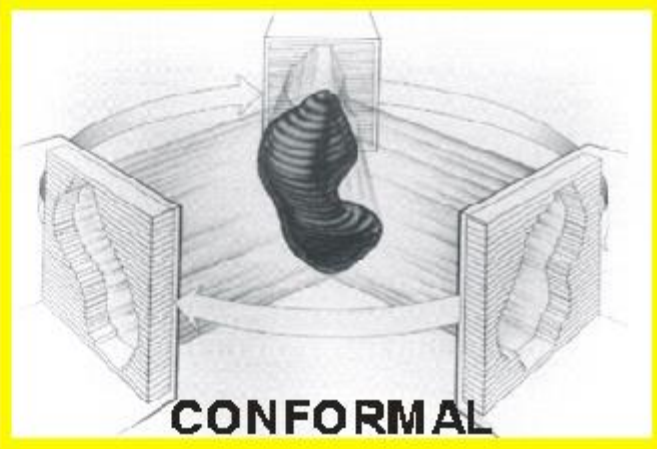
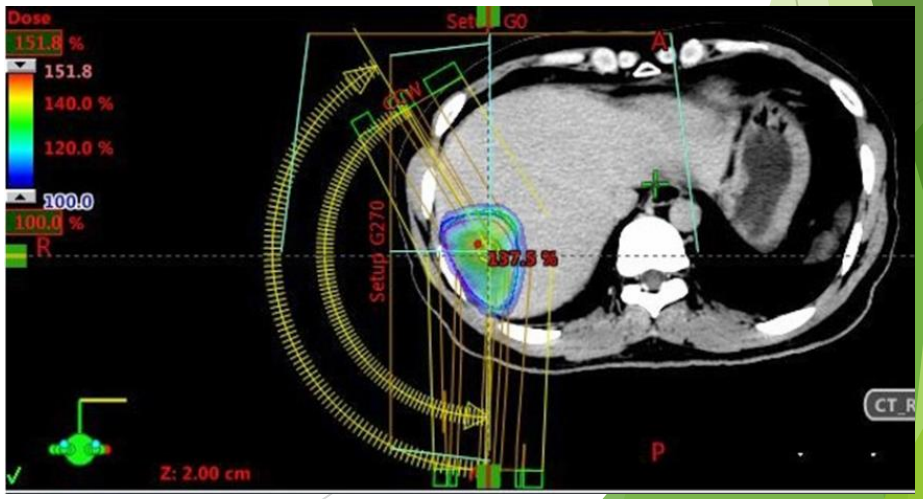
SBRT for HCC—myths
Too toxic (improved conformality)



IMRT(Intensity Modulated Radiotherapy)**/VMAT**(Volumetric Modulated Arc Therapy)



What is SBRT?

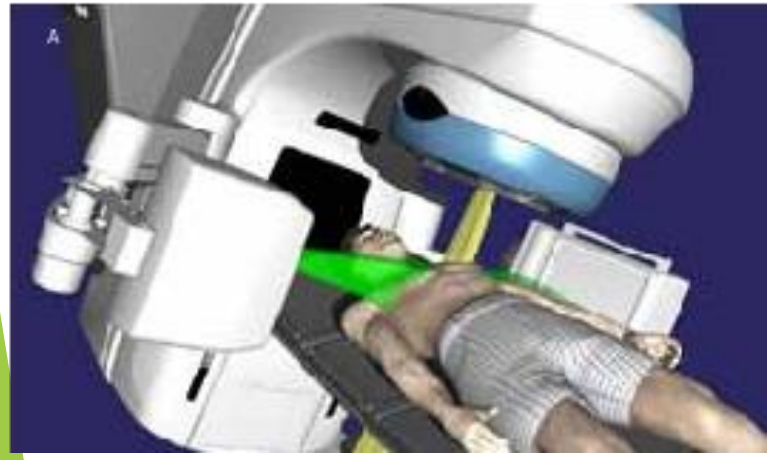
1)Thin cut planning CT
2)Respiratory motion control

1)Treatment planning with IMRT
2) Co-registration with MRI/PET

Additional Quali
Assurance proce
by physicists

1) IGRT: Verification using cone beam CT
2) RT delivered by IMRT/VMAT
3) Respiratory motion control

Daily CBCT verification



SBRT for HCC—published evidence

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HyTEC Organ-Specific Paper: Abdomen and Pelvis

Local Control After Stereotactic Body Radiation Therapy for Liver Tumors

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SBRT for HCC—published evidence

Table 1 Characteristics of the 13 studies included in the present analysis

First author (country) (reference)	Disease	Sample size	SBRT schedule	Prescription point/volume	Median (range) follow-up
Dewas (France) (17)	HCC	42 patients,* 48 lesions*	Median 45 Gy, 3 fx	PTV (80% IDL)	15 mo
Honda (Japan) (26)	HCC	30 patients*	Median 48 Gy, 4 fx	Isocenter	12 (6-38) mo
Jang (Korea) (24)	HCC	82 patients, 95 lesions	<45 Gy, 3 fx (n = 11) 45-54 Gy, 3 fx (n = 47) >54 Gy, 3 fx (n = 57)	PTV (70-80% IDL)	30 (4-81) mo
Kwon (Korea) (18)	HCC	42 patients	Median 33 Gy, 3 fx	PTV (70-85% IDL)	29 (8-49) mo
Sanuki (Japan) (25)	HCC	185 patients	35 Gy, 5 fx (n = 48) 40 Gy, 5 fx (n = 137)	PTV (70-80% IDL)	25† (3-80) mo
Barney (United States) (19)	CCA	9 patients,* 10 lesions*	45-60 Gy, 3-5 fx	NR	14 (2-26) mo
Kopek (Denmark) (23)	CCA	27 patients	45 Gy, 3 fx	Isocenter	5.4 (2.3-8.6) y
Mendez Romero (The Netherlands) (20)	Mets (82% CRC)	17 patients,* 34 lesions*	Median 37.5 Gy, 3 fx	PTV (65% IDL)	13 (1-31) mo
Rusthoven (United States) (27)	Mets (32% CRC, 21% lung)	36 patients,* 49 lesions*	60 Gy, 3 fx	PTV (80-90% IDL)	16 (6-54) mo
Scorsetti (Italy) (28)	Mets (48% CRC)	61 patients, 76 lesions	75 Gy, 3 fx	PTV	12 (2-26) mo
Stintzing (Germany) (21)	Mets (100% CRC)	30 patients, 35 lesions	24-26 Gy, 1 fx	70% IDL	35 (6-96) mo
Vautravers-Dewas (France) (22)	Mets (67% CRC)	42 patients, 62 lesions	40 Gy, 4 fx (n = 29) 45 Gy, 3 fx (n = 16)	80% IDL	14 (2-23) mo
Wulf (Germany) (29)	Mets (45% CRC)	39 patients, 51 lesions	Median 30 Gy, 3 fx (n = 25) Median 37.5 Gy, 3 fx (n = 26)	PTV (65% IDL)	15 (2-85) mo

Abbreviations: CCA = cholangiocarcinoma; CRC = colorectal cancer; fx = fractions; HCC = hepatocellular carcinoma; IDL = isodose line; Mets = liver metastases; NR = not reported.

* Subset of larger cohort included in present analysis.

† Estimate.

SBRT for HCC—published evidence

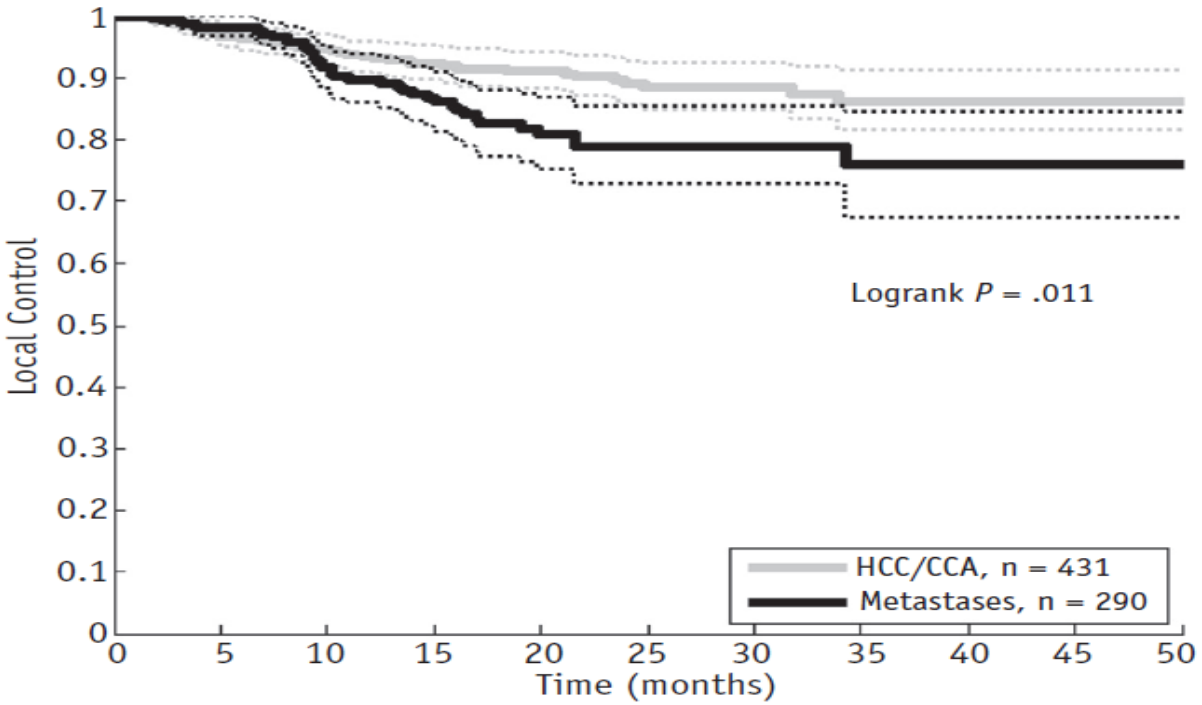
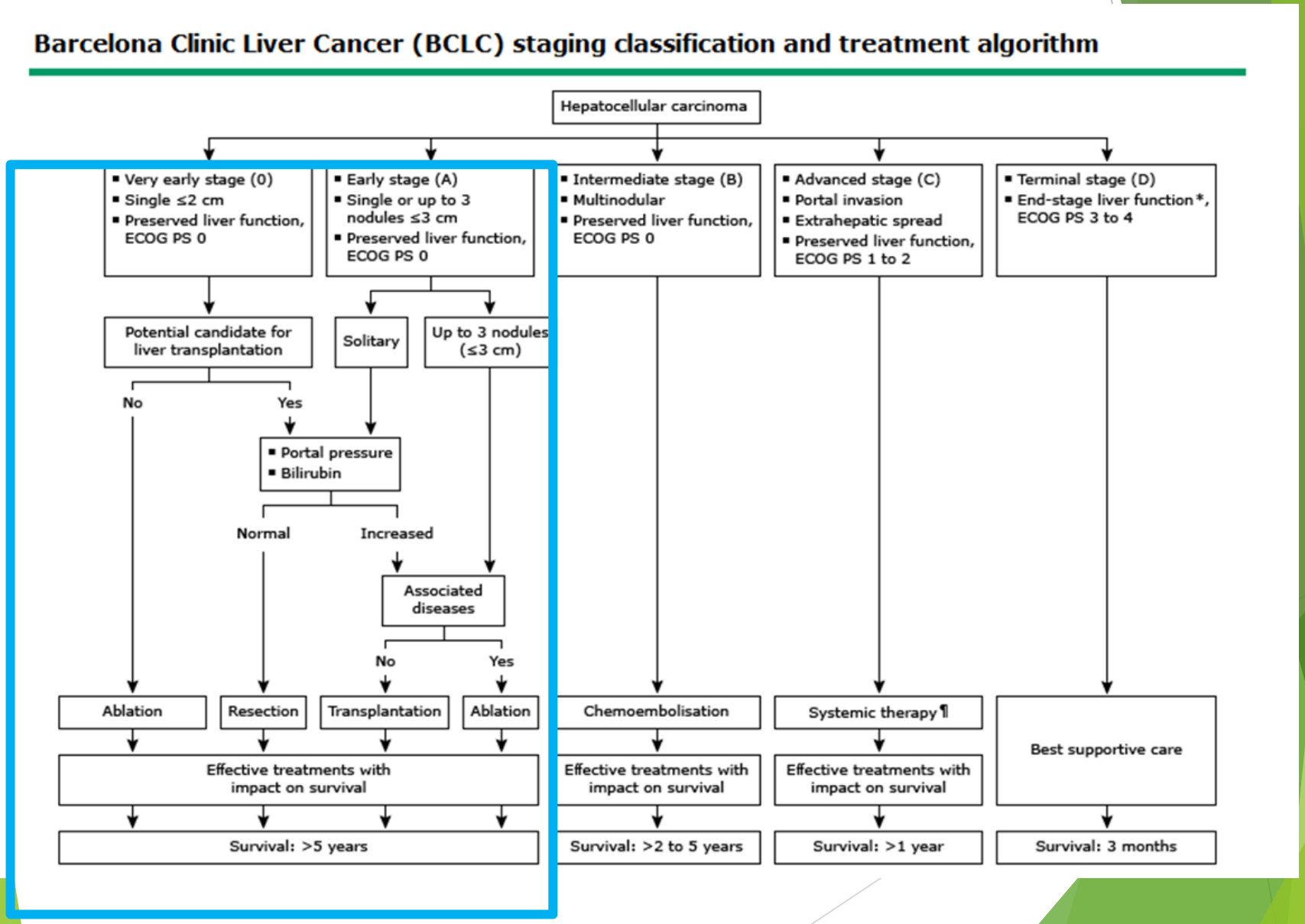


Fig. 1. Kaplan-Meier curves for local control of primary and metastatic liver tumors after stereotactic body radiation therapy. *Abbreviations:* CCA = cholangiocarcinoma; HCC = hepatocellular carcinoma.

Liver cancer—treatment option by stage



SBRT for HCC—published evidence

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JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

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

See accompanying article on page 404

Daniel R. Wahl, Matthew H. Stenmark, Yebin Tao, Erqi L. Pollom, Elaine M. Caoili, Theodore S. Lawrence, Matthew J. Schipper, and Mary Feng, University of Michigan Medical Center; and Matthew H. Stenmark, Veterans Affairs Medical Center, Ann Arbor, MI.

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D.R.W. and M.H.S. contributed equally to this work.

Authors' disclosures of potential conflicts of interest are found in the article online at www.jco.org. Author contributions are found at the end of this article.

A B S T R A C T

Purpose

Data guiding selection of nonsurgical treatment of hepatocellular carcinoma (HCC) are lacking. We therefore compared outcomes between stereotactic body radiotherapy (SBRT) and radiofrequency ablation (RFA) for HCC.

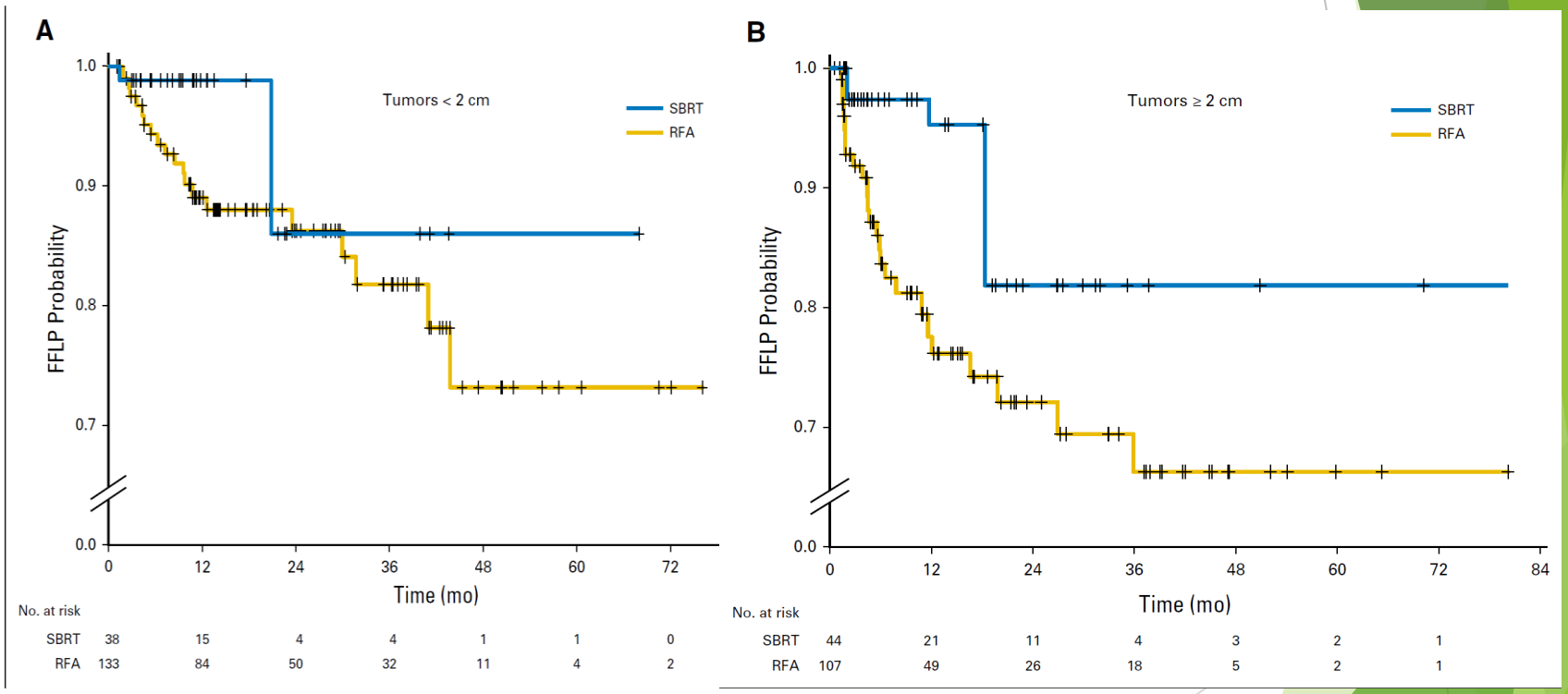
Patients and Methods

From 2004 to 2012, 224 patients with inoperable, nonmetastatic HCC underwent RFA (n = 161) to 249 tumors or image-guided SBRT (n = 63) to 83 tumors. We applied inverse probability of treatment weighting to adjust for imbalances in treatment assignment. Freedom from local progression (FFLP) and toxicity were retrospectively analyzed.

Results

RFA and SBRT groups were similar with respect to number of lesions treated per patient, type of underlying liver disease, and tumor size (median, 1.8 *v* 2.2 cm in maximum diameter; $P = .14$). However, the SBRT group had lower pretreatment Child-Pugh scores ($P = .003$), higher pretreatment alpha-fetoprotein levels ($P = .04$), and a greater number of prior liver-directed treatments ($P <$

SBRT for HCC—published evidence



SBRT for HCC—published evidence

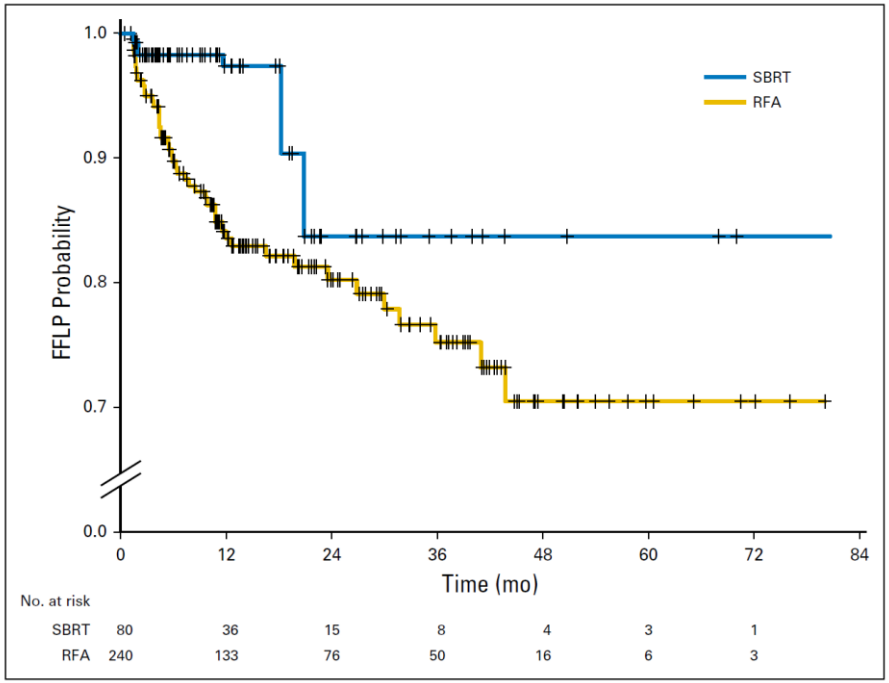
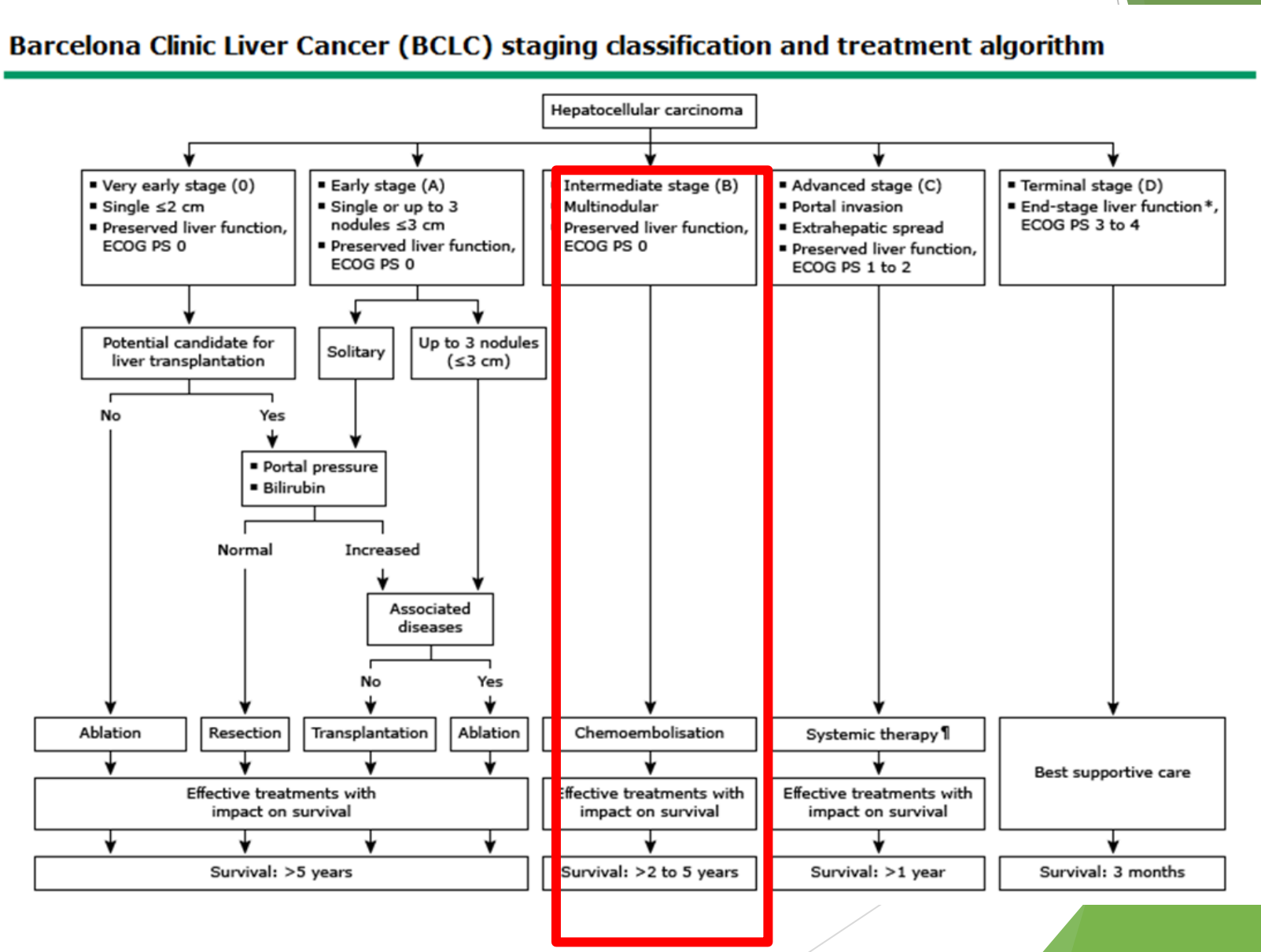


Fig 1. Freedom from local progression (FFLP) by treatment modality. RFA, radiofrequency ablation; SBRT, stereotactic body radiotherapy.

SBRT for HCC—published evidence

toxicities	RFA	SBRT
Grade 3+ adverse event	11%	5% (P = .31 v RFA)
	1pneumothorax ,2 sepsis,2 duodenal and colonic perforation , 3 bleeding	1 radiation-induced liver disease ,1 GI bleeding and 1 worsening ascites
Deaths	2 deaths within 1 month of treatment (1 hemothorax, 1 GI bleeding)	No deaths were seen as a consequence of SBRT
Grade 3 biliary toxicities	at 1 year 2.3%, at 2 years 6%	3.3% (P = .7) 3.3% (P = .38)
Grade 3 luminal GI toxicites	At 1 year 3.4% At 2 year 6.4%	5.4%(p=0.49) 8.3% (p=0.66)

Liver cancer—treatment option by stage



SBRT for HCC—published evidence

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Clinical Investigation

Stereotactic Body Radiation Therapy as an Alternative to Transarterial Chemoembolization for Hepatocellular Carcinoma

Eli Sapir, MD,*,† Yebin Tao, PhD,‡ Matthew J. Schipper, PhD,‡ Latifa Bazzi, BA,* Paula M. Novelli, MD,§ Pauline Devlin, MS,‖ Dawn Owen, MD,* Kyle C. Cuneo, MD,* Theodore S. Lawrence, MD, PhD,* Neehar D. Parikh, MD,‖ and Mary Feng, MD*,¶

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SBRT for HCC—published evidence

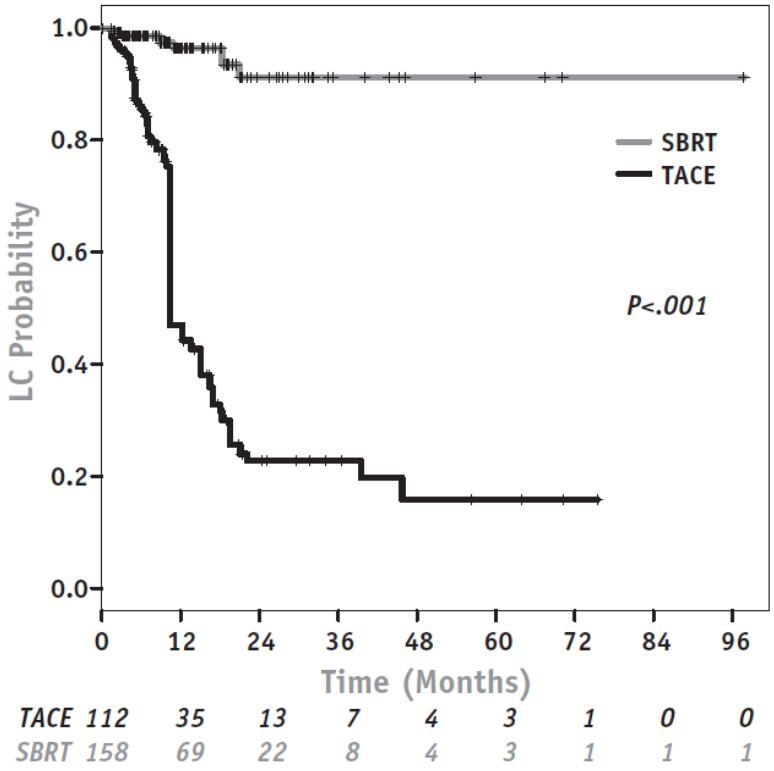

Fig. 1. Local control (LC) by treatment modality. *Abbreviations:* SBRT = stereotactic body radiation therapy; TACE = transarterial chemoembolization.

SBRT for HCC—published evidence

	TACE	SBRT
G3 events	13%	8% (p=0.05)
	severe hypervolemia after TACE ,acute cholecystitis , severe anasarca associated with hypovolemic renal failure , biliary abscess , hepatic artery injury , biliary stricture , upper GI bleeding caused by gastric ulcer , severe hyperkalemia with a non-ST-elevated myocardial infarction immediately after TACE	biliary strictures , upper GI bleeding associated with gastric or duodenal ulcer ,bleeding from esophageal varices and severe hypervolemia after SBRT **One patient developed radiation induced liver disease.**

SBRT for HCC—published evidence (local data)

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Better survival after stereotactic body radiation therapy following transarterial chemoembolization in nonresectable hepatocellular carcinoma: A propensity score matched analysis

Tiffany CL. Wong[a,b], Chi-Leung Chiang[c,d,e], Ann-Shing Lee[e], Victor HF. Lee[c,d], Cynthia SY. Yeung[e], Connie HM. Ho[e], Tan-To Cheung[a,b], Kelvin KC. Ng[a,b], Siu-Ho Chok[a,b], Albert CY. Chan[a,b], Wing-Chiu Dai[a,b], Frank CS. Wong[e], Mai-Yee Luk[c,d], To-Wai Leung[c,d], Chung-Mau Lo[a,b,*]

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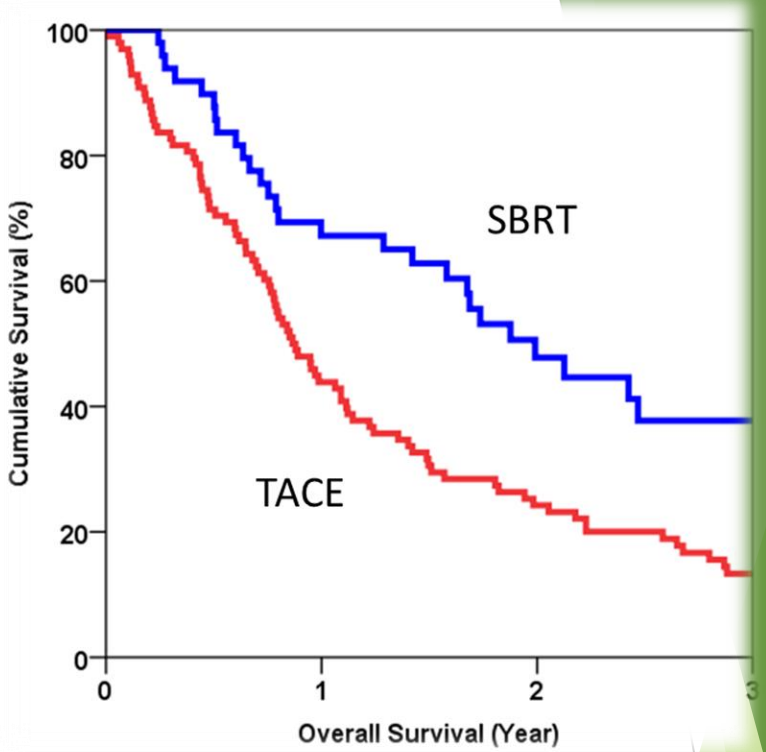
TACE + SBRT vs TACE alone

- Retrospective comparison with propensity score matching
- 2011- 2014
- Unresectable HCC of Intermediate stage

Baseline characteristics of all patients			
	TACE N=98	TACE + SBRT N=49	P value
PVT	0 (0)	0 (0)	-
No. of tumor Solitary Multiple	 56 (57.1%) 42 (42.9%)	 27 (55.1%) 22 (44.9%)	0.81
Number of lesion Solitary Two Three Multiple	 56 (57.1%) 13 (13.3%) 2 (2%) 27 (27.6%)	 27 (55.1%) 7 (14.3%) 5 (10.2%) 10 (20.4%)	0.15
Size of the largest tumor (cm)	10.1 (1.8-22.4)	9.5 (4-23.6)	0.89
UICC 7th edition Stage I Stage II Stage IIIA Stage IIIB Stage IIIC Stage IVA	 50 (51%) 2 (2%) 35 (35.7%) 1 (1%) 7 (7.1%) 3 (3.1%)	 16 (32.7%) 1 (2%) 26 (53.1%) 2 (4.1%) 2 (4.1%) 2 (4.1%)	0.27

TACE + SBRT
vs
TACE alone

- Retrospective comparison with propensity score matching
- 2011- 2014
- Unresectable HCC of Intermediate stage



	TACE alone	TACE+SBRT	
N	98	49	
OS	10.4 m	23.9 m	P 0.001
1 yr	43.9%	67.2%	
3 yr	13.3%	37.8%	
5 yr	6.4%	14.4%	

TACE + SBRT
vs
TACE alone

- Retrospective comparison with propensity score matching
- 2011- 2014
- 98(QMH)+49(TMH) patients
- Unresectable HCC of Intermediate stage

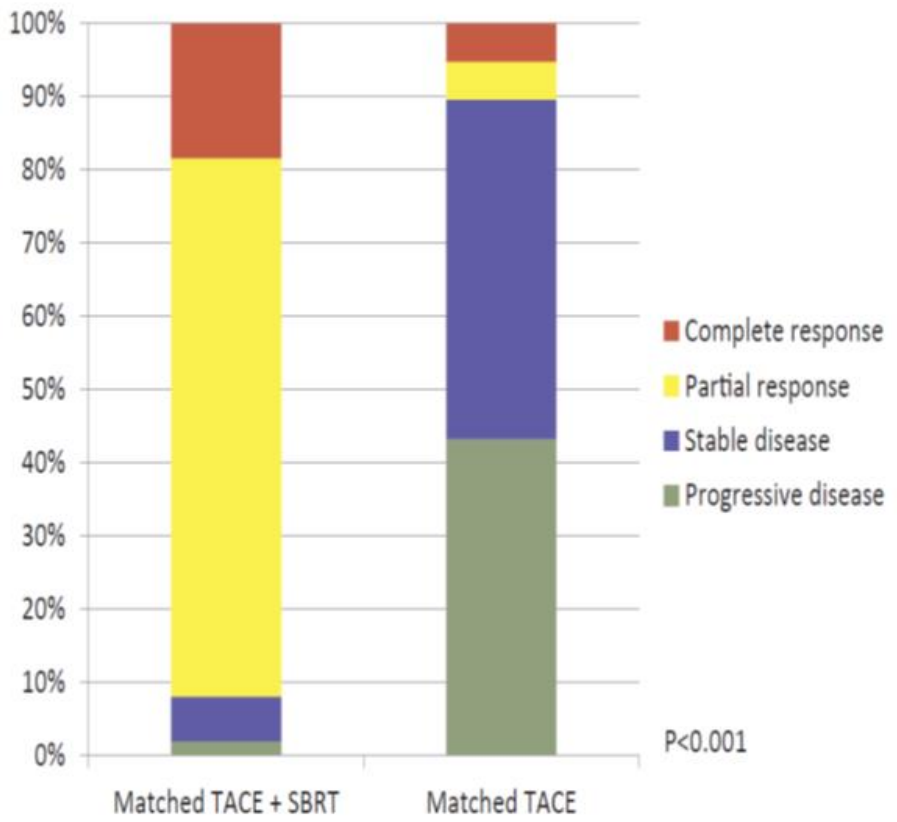


Fig. 2. The best mRECIST of matched TACE and matched TACE + SBRT patients.
b. The trend of AFP before and after treatment for matched TACE and matched TACE + SBRT patients.

SBRT for HCC –published evidence (local data) Safety

Table 3
Treatment toxicity of all patients after propensity score matching.

Parameters (n,%)	Matched TACE (n = 98)	Matched TACE + SBRT (n = 49)	*p* value
Fatigue			
0	67 (69.1)	21 (42.9)	< 0.001
1	24 (24.7)	10 (20.4)	
2	6 (6.2)	18 (36.7)	
≥3	0	0	
Fever			
0	78 (80.4)	42 (85.7)	0.008
1	19 (19.6)	4 (8.2)	
2	0	3 (6.1)	
≥3	0	0	
Bilirubin			
0	55 (56.7)	20 (40.8)	0.036
1	19 (19.6)	17 (34.7)	
2	16 (16.5)	6 (12.2)	
≥3	7 (7.2)	6 (12.2)	
Albumin			
0	10 (10.3)	33 (67.3)	< 0.001
1	53 (54.6)	7 (14.3)	
2	34 (35.1)	9 (18.4)	
≥3	0	0	
AST			
0	10 (10.3)	25 (51)	< 0.001
1	41 (42.3)	10 (20.4)	
2	32 (33)	5 (10.2)	
≥3	14 (14.4)	9 (18.4)	
INR			
0	62 (63.9)	48 (98)	< 0.001
1	32 (33)	1 (2)	
2	2 (2.1)	0	
≥3	1 (1)	0	
Platelet			
0	59 (60.8)	20 (40.8)	0.021
1	31 (32)	17 (34.7)	
2	4 (4.1)	8 (16.3)	
≥3	3 (3.1)	4 (8.2)	
White cell			
0	88 (90.7)	33 (67.3)	0.001
1	8 (8.2)	8 (16.3)	
2	1 (1)	7 (14.3)	
≥3	0 (0)	1 (2)	
Hemoglobin			
0	97 (100)	30 (61.2)	< 0.001
1	0	10 (20.4)	
2	0	6 (12.2)	
≥3	0	3 (6.1)	
Creatinine			
0	69 (71.1)	44 (89.8)	0.017
1	20 (20.6)	5 (10.2)	
2	5 (5.2)	0	
≥3	3 (3.1)	0	

TACE + SBRT group, p = 0.190). At 1 month after completion of treatment, in the matched TACE group, 45/98 (46.4%) patients were Child's A and 44/98 (57.1%) were Child's B. In the TACE + SBRT group, 20/49 (40.8%) and 28/49 (57.1%) were Child's A and B respectively at 1 month after treatment and there was no difference between the 2 groups (p = 0.168). None developed classical RILD