# Strahlentherapie bei Lebertumoren: Eine unterschätzte Option?

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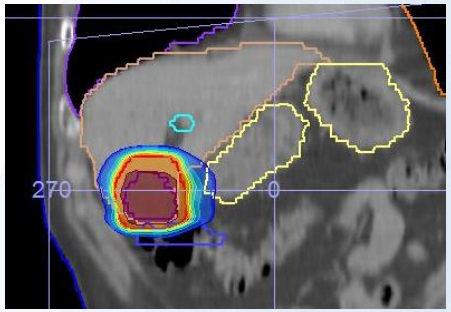
*Klinik für Strahlentherapie und Radioonkologie, Mannheim*

DGHO,
Hamburg, 2023



# How it started…

**1994**:

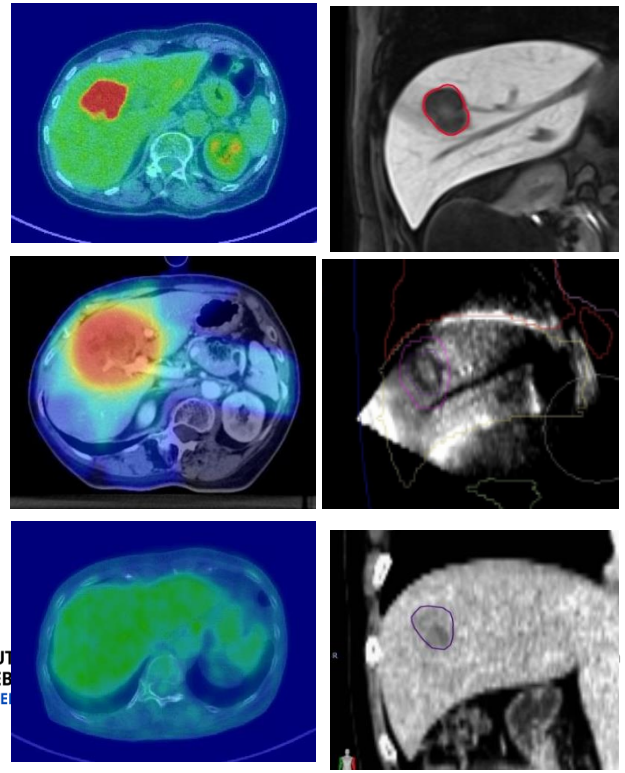
- keine online Bildgebung
- nur 2D Verifikation
- 3D Felder
- keine Bewegungskompensation
- suboptimale prä-RT Bildgebung
- Normalgewebstoleranz?

Stereotactic Body Frame, Lax *et al.*

# How it`s going…

**2023:**

- online 3D Bildgebung, präzise Applikation
- hohe Einzeldosen mit steilen Dosisgradienten
- Atemgating /Tracking
- optimale prätherapeutische Bildgebung (MRT, PET..)
- exakte Kenntnisse, internationale Guidelines für SBRT

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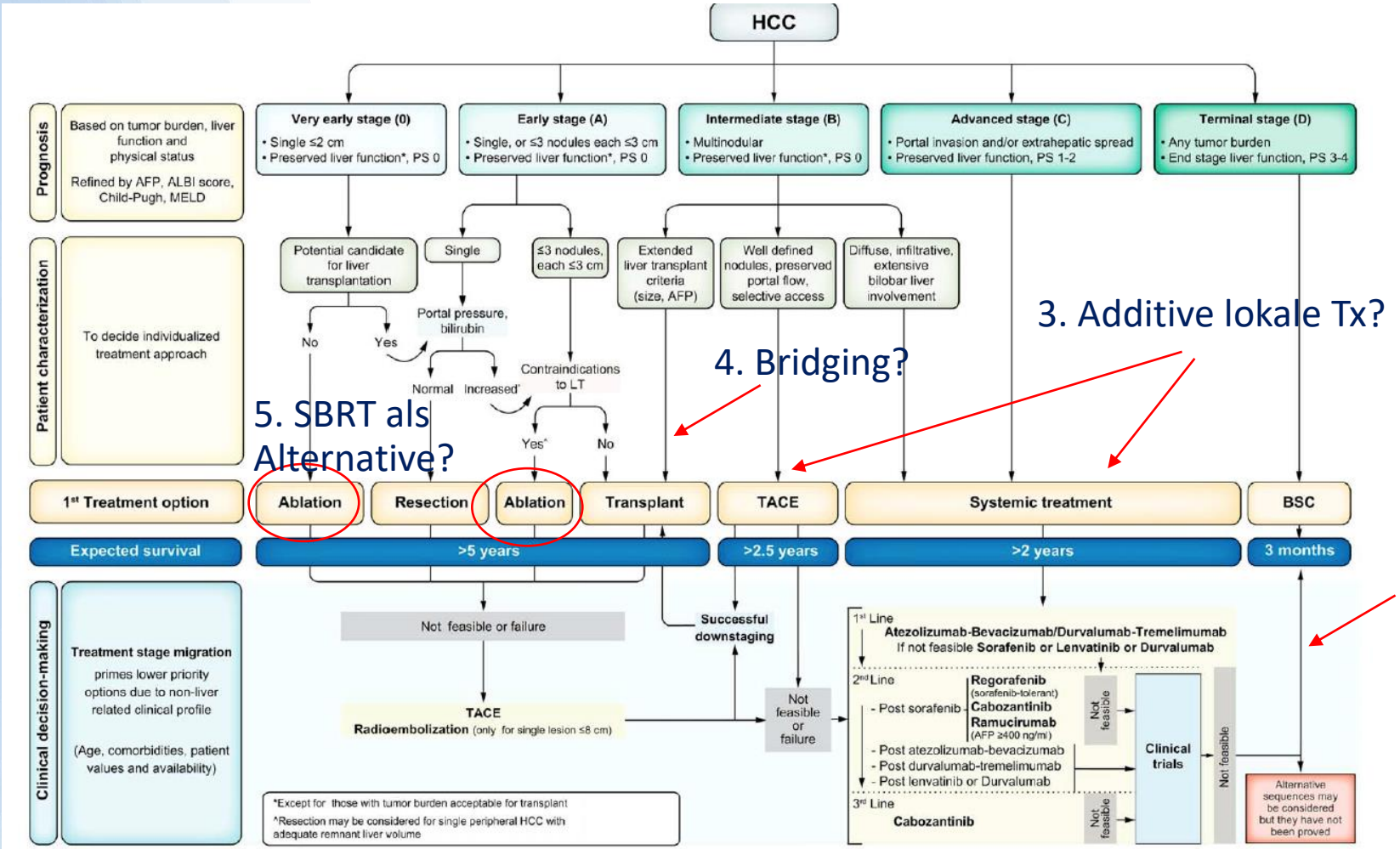
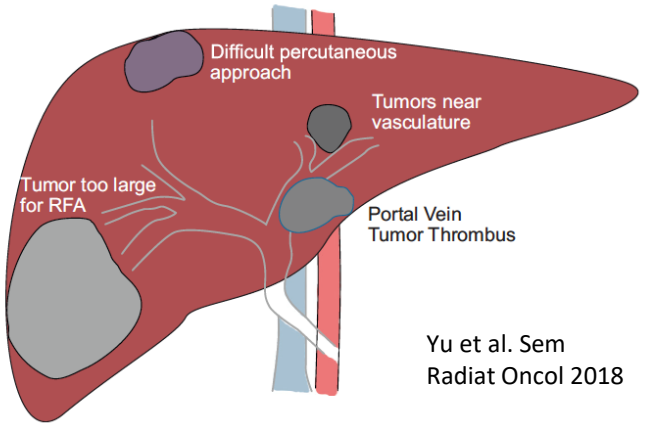
dkfz. DEUT KREB IN DE

# AASLD Practice Guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma

DOI: 10.1097/HEP.0000000000000466

Amit G. Singal[1] | Josep M. Llovet[2,3,4] | Mark Yarchoan[5] | Neil Mehta[6] | Julie K. Heimbach[7] | Laura A. Dawson[8] | Janice H. Jou[9] | Laura M. Kulik[10] | Vatche G. Agopian[11] | Jorge A. Marrero[12] | Mishal Mendiratta-Lala[13] | Daniel B. Brown[14] | William S. Rilling[15] | Lipika Goyal[16] | Alice C. Wei[17] | Tamar H. Taddei[18,19]




Yu et al. Sem Radiat Oncol 2018

3. Additive lokale Tx?

4. Bridging?

5. SBRT als Alternative?

1. Palliation/Symptomkontrolle?

2. Oligometastasen- Metastasen-Kontrolle?

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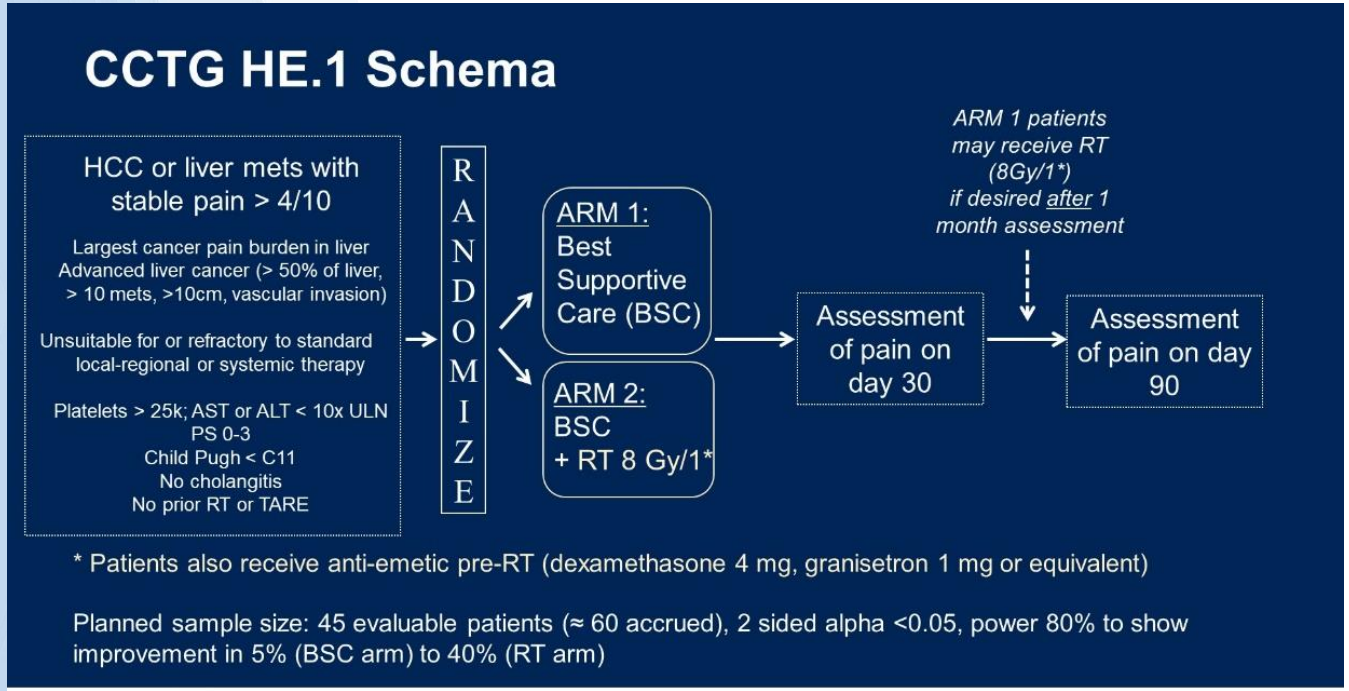
# 1. Palliativ - Symptomkontrolle

## CCTG HE.1: RT für symptomatische HCC/mets




ASCO GI 2023; Congess Slides Prof. Dawson, posted on X by Dr. Stanford N. for @OncoAlert

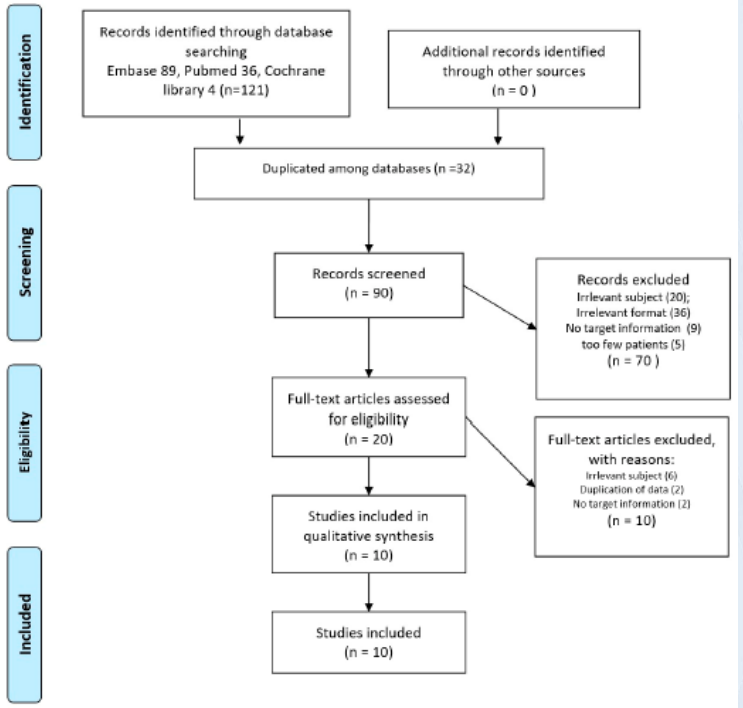
- Phase III (Canada), NCT02511522
- Palliative RT vs. BSC
- 43 Metastasen, 23 HCC
- ECOG 2-3
- 64% CP A
- Baseline Schmerz 7/10
- Endpunkt: Schmerzreduktion
- Große Zielvolumina (3600ml im Median), 1x8Gy + Antiemese/FC
- -> signifikantes Schmerz-Ansprechen
- -> 3-Monate OS 33 vs. 51%

# 2. Oligometastasiertes HCC

*Cancers* **2023**, *15*, 3467. https://doi.org/10.3390/cancers15133467

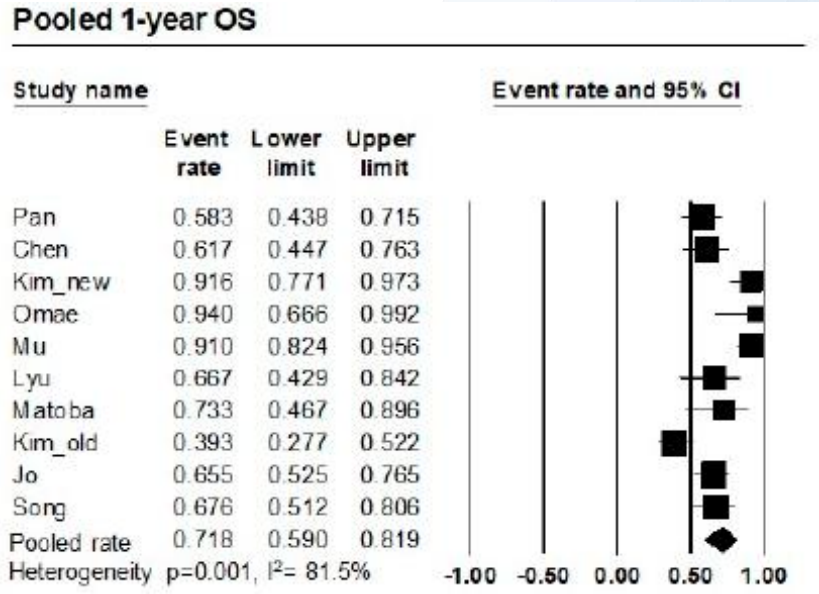
## Local Treatment of Hepatocellular Carcinoma with Oligometastases: A Systematic Review and Meta-Analysis

Sooyeon Kim [1,†], Jungsue Lee [1,†] and Chai Hong Rim [1,2,*]




- Oligomets: LN, Lunge, NN, Knochen
- Lokale Therapiemodalitäten: RFA, OP, (hypofraktionierte) RT, SBRT
- Metaanalyse mit Suche bis 2022 (10 Studien), Endpunkt: OS
- Onkologischer Benefit konsistent in der gepoolten Analyse
- Gepoolte Überlebensdaten vorteilhaft im Vergleich zu der hist. Literatur
- Keine relevante Erhöhung der Toxizität
- Diese systematische Review ist eine Basis für die Verwendung lokaler Therapiestrategien bei Oligometastasen

| Author | No. of Patients | Study Design | Treatment Method | Primary Controlled | Follow-Up Period | Overall Survival (M, Median) | Factors Affecting Survival | Toxicity (Grade ≥ 3) |
|---|---|---|---|---|---|---|---|---|
| Jo | 58 | Case series | SBRT (chemotherapy, 36.2%) | | | MOS 16.3 months (1/2y: 65.5, 41.4%) MPFS 4.9 months (1/2y: 22.4, 13.5%) | CPC, Controlled primary disease, RT response | 3 cases of grade 4 Leukopenia (5.2%); 2 cases of grade 3 pneumonia (3.4%), 1 case of leukopenia (1.7%), 1 case of dermatitis (1.7%) |
| Song | 37 | Case series | SBRT | | 19.9 | M19.9 months 1/3y: 67.6/35.5 | Treatment modality | No significant RT complication |



# 3. HCC - lokale Ablation

Leitlinienprogramm Onkologie

**Diagnostik und Therapie des Hepatozellulären Karzinoms und biliärer Karzinome**

Version 4.0 – August 2023
AWMF-Registernummer: 032-053OL

### 3.4.3 Stereotaxie

| 3.66 | Evidenzbasierte Empfehlung | modifiziert 2023 |
|---|---|---|
| Empfehlungsgrad **B** | Eine Hochpräzisionsradiotherapie (Stereotactic Body Radiotherapy; SBRT) sollte geprüft werden, wenn andere lokale Therapieverfahren nicht oder nur mit Einschränkungen möglich sind. | |
| Level of Evidence **2** | [327], [328], [329]. [330]. [331]. [332]. | |
| | Konsens (88% Zustimmung (84% Zustimmung unter Mitberechnung der Enthaltungen aufgrund von Interessenkonflikten) | |

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# Retrospektive Studien - Limitationen

JHEP Reports **2019** vol. 1 | 131–137

## Radiotherapy for HCC: Ready for prime time?

Andrew Bang,[1] Laura A. Dawson[1,*]

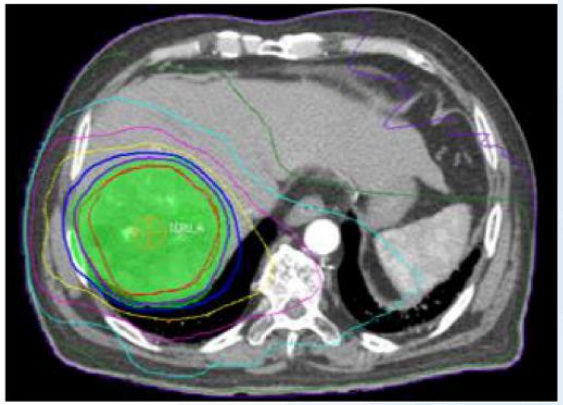
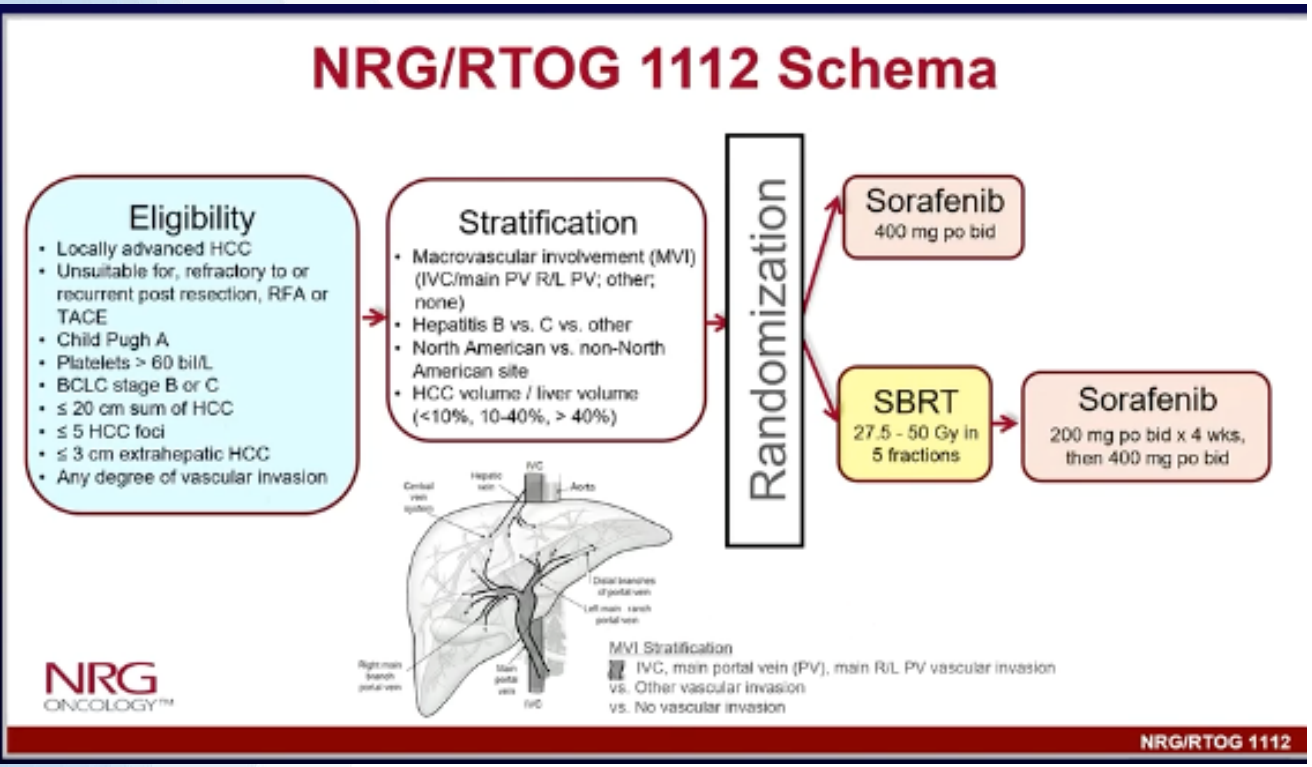



**Table 1. Selected prospective studies.**

| Study | Median follow-up, months (range) | CP score | Tumour vascular thrombosis | Extrahepatic disease | Median length or volume (range) | Dose/ fractionation | Acute grade 3+ GI or liver toxicity | Local control | Overall survival |
|---|---|---|---|---|---|---|---|---|---|
| Feng (2018) n = 90 [19] | 37 | A: 77% B: 23% | 18% | 19% | 3 cm (0–13 cm) | 23 Gy/5–60 Gy/5 | 7% | 2-yr: 95% | n.a. |
| Kim (2018) n = 32 [20] | 27 (12–55) | A: 88% B: 12% | 0% | 0% | 2.1 cm (1.0–4.5 cm) | 36 Gy/4–60 Gy/4 | 0% | 2-yr: 81% | 2-yr: 81% |
| Moon (2018) n = 30 [21] | 12.7 | A: 93% B: 7% | – | 18% | 22.5 $cm^3$ (2.8–145 $cm^3$) | 27.5 Gy/5–45 Gy/3 | 7% | 1-yr: 81% | 1-yr: 36% |
| Takeda (2016) n = 90 [22] | 41.7 (6.8–96.2) | A: 91% B: 9% | 3% | 0% | 2.3 cm (1.0–4.0 cm) | 35 Gy/5–40 Gy/5 | 11% | 3-yr: 96% | 3-yr: 67% |
| Lasley (2015) n = 59 [23] | CPA: 33.3 CPB: 46.3 | A: 64% B: 36% | 20% | 0% | 33.6 $cm^3$ (2–107 $cm^3$) | 40 Gy/5–48 Gy/3 | 20% | 3-yr: A: 91% B: 82% | 3-yr: A: 61% B: 26% |
| Scorsetti (2015) n = 43 [24] | 8 (3–43) | A: 53% B: 47% | 20% | 4% | 4.8 cm (1–13 cm) | 36 Gy/6–75 Gy/3 | 16% | 1-yr: 86% 2-yr: 64% | 1-yr: 78% 2-yr: 45% |
| Bujold (2013) n = 102 [18] | 31.4 | A: 100% | 55% | 12% | 117 $cm^3$ (1–1,913 $cm^3$) | 24 Gy/6–54 Gy/6 | 30% | 1-yr: 87% | Median: 17 months |
| Kang (2012) n = 47 [25] | 17 (6–38) | A: 87% B: 13% | 11% | 0% | 2.9 cm (1.3–7.8 cm) | 42 Gy/3–60 Gy/3 | 6.4% | 2-yr: 95% | 2-yr: 69% |
| Mendez–Romero (2006) n = 8 [26] | 13 (1–31) | A: 63% B: 25% | 38% | 0% | 3.5 cm (0.5–7.2 cm) | 25 Gy/5–37.5 Gy/3 | 12.5% | 1-yr: 75% | 1-yr: 75% 2-yr: 40% |

ASTRO 2022, Dawson et al., congress abstract
Watcharawipha et al., 2023; Craig et al., 2023

# RTOG 1112: Systemtherapie +/- SBRT, Ph. III




- Vorzeitig geschlossen (veränderte Systemtherapie-Landschaft)
- 193 Pat randomisiert

- Median OS 12 vs. 15.8 Monate (p=0.055)
- Median PFS 5.5 vs. 9 Monate (p=0.0001)
- TTP 9.5 vs. 18.5 Monate! (p=0.034)

- 82% BCLC-C, 63% MVI, große Tumore (8cm DM)
- 20-50Gy in 2-5F (angepasst an Risikoorgan-Dosen)
- Keine erhöhte Toxizität bei Addition von SBRT

Landmark Studie, jedoch:

? Rolle der SBRT in Immuntherapie-Ära?
-> Neue Studien notwendig, e.g. Atezo/Beva +/- SBRT

# SBRT versus andere lokal ablative Therapien: SBRT vs. RFA

Radiofrequency Ablation Versus Stereotactic Body Radiotherapy for Localized Hepatocellular Carcinoma in Nonsurgically Managed Patients: Analysis of the National Cancer Database

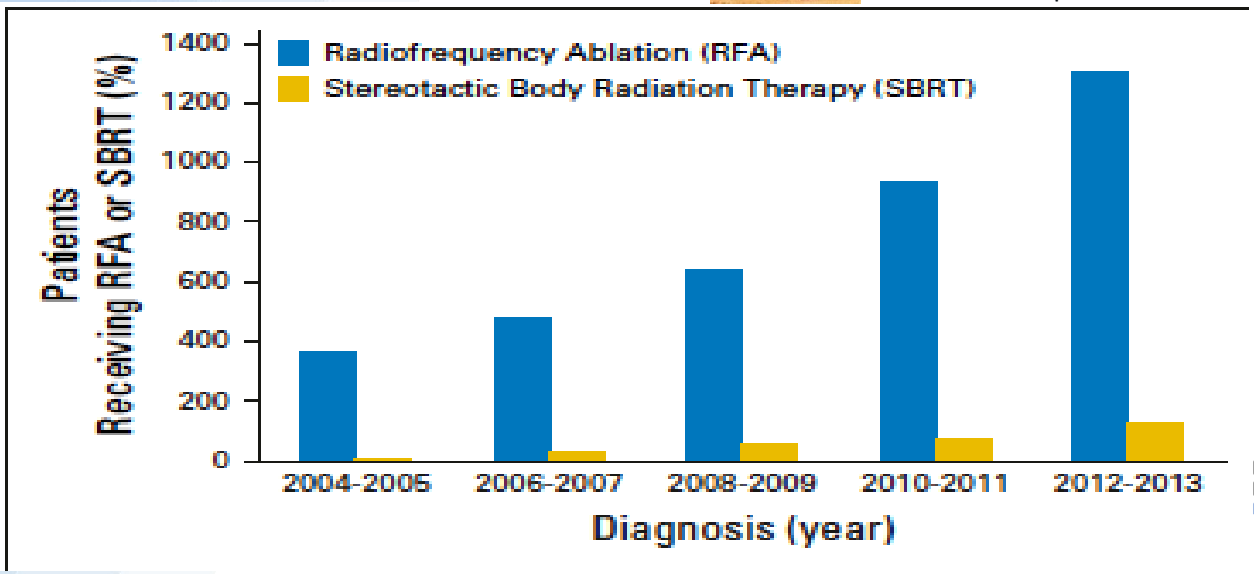
*J Clin Oncol 36. © 2018 by American Society of Clinical Oncology*

*Devalkumar J. Rajyaguru, Andrew J. Borgert, Angela L. Smith, Reggie M. Thomes, Patrick D. Conway, Thorvardur R.*

n= 296 SBRT (7%)

n= 3684 RFA (93%)

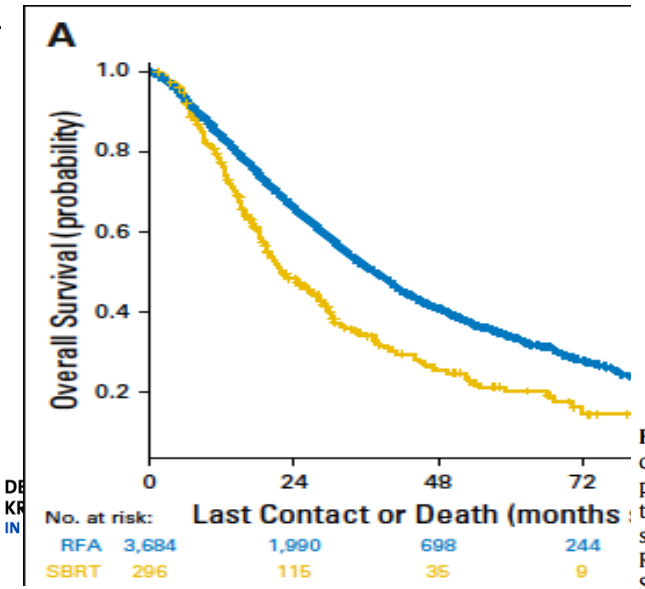
Tori Sumo fun pictures




- SBRT Patn sign. Älter – Patientenseletion…
- Tumor größer
- Ishak Fibrosis fortgeschrittener….

- Keine Daten bezüglich lokale Kontrolle und Technik
- Keine Daten zu **Child-Turcotte-Pugh** score
- **fehlende BCLC Stadium** und Daten bzgl. MVI
- Ausschluss von Patients mit neoadj./adj. Tx oder vorherige andere lokalablative Therapien

https://doi.org/10.1016/j.clon.2023.07.002



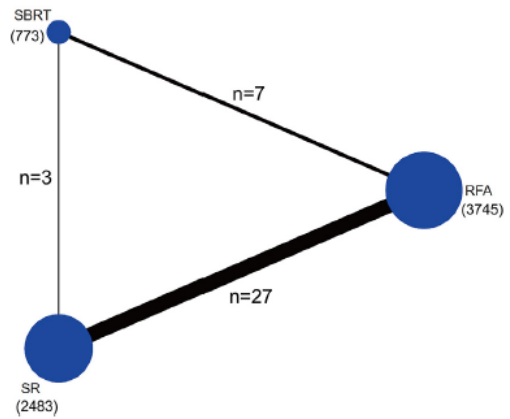



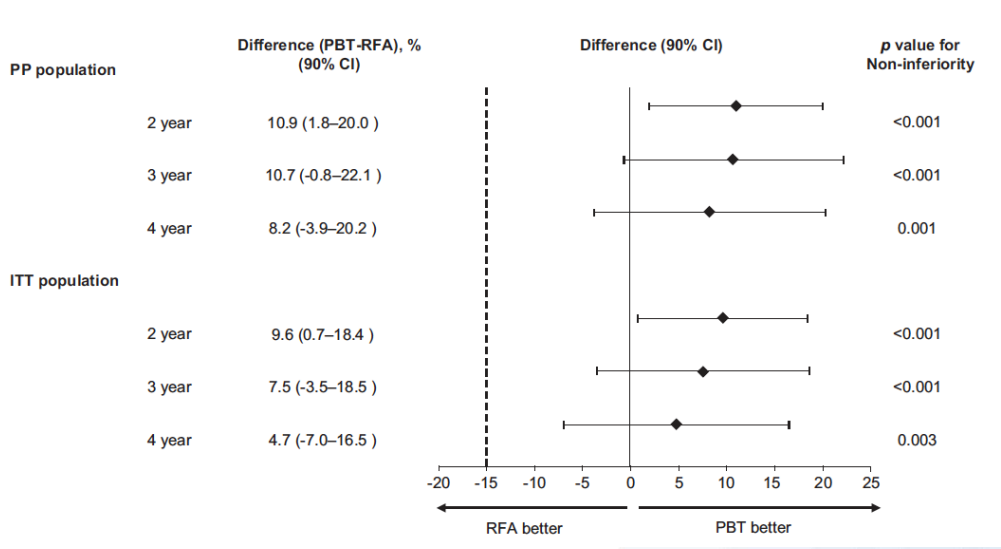

**Fig 2.** Network of comparisons for overall survival generated by a comparative network meta-analysis. The size of the nodes is proportional to the number of patients (in parentheses) receiving the treatment. The width of the lines is proportional to the number of studies (adjacent to the line) comparing the connected treatments. RFA, radiofrequency ablation; SBRT, stereotactic body radiotherapy; SR, surgical resection.

# RT (PBT) vs. RFA

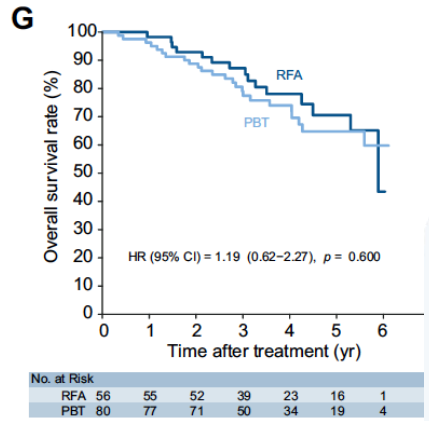
Journal of Hepatology **2021** vol. 74 | 603–612

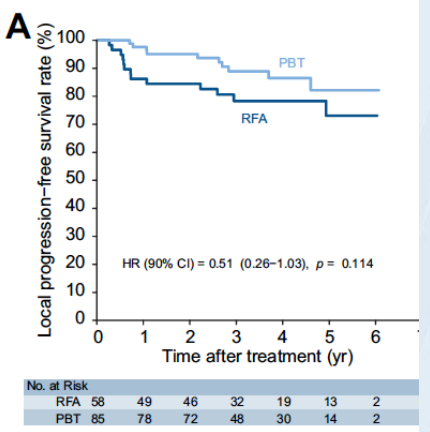
## Proton beam radiotherapy *vs.* radiofrequency ablation for recurrent hepatocellular carcinoma: A randomized phase III trial

Tae Hyun Kim[1,2,†], Young Hwan Koh[1,3,†], Bo Hyun Kim[1], Min Ju Kim[3], Ju Hee Lee[1,3], Boram Park[4], Joong-Won Park[1,*]




- Phase III, noninferiority RCT
- Patienten mit HCC (recurrent/residual)
- Nichtunterlegenheit bzgl. 2J lokale PFS (92.8% vs. 83.2%)
- weniger Patienten mit Child-Turcotte-Pugh Score Erhöhung nach Therapie (7.5% vs. 19.6%)

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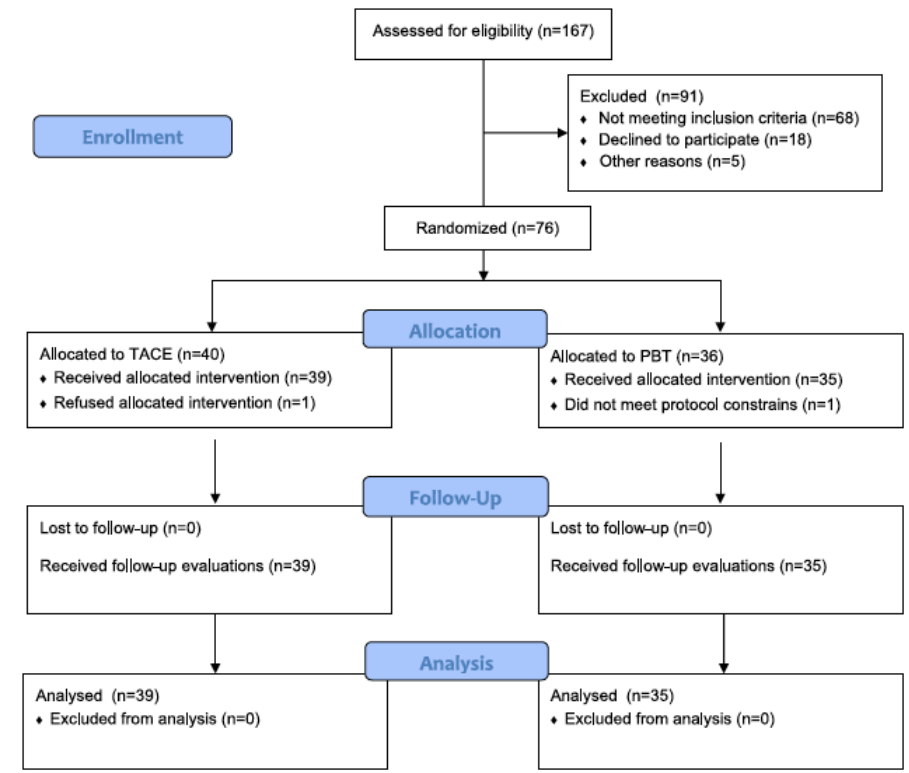
# RT (PBT) vs. TACE

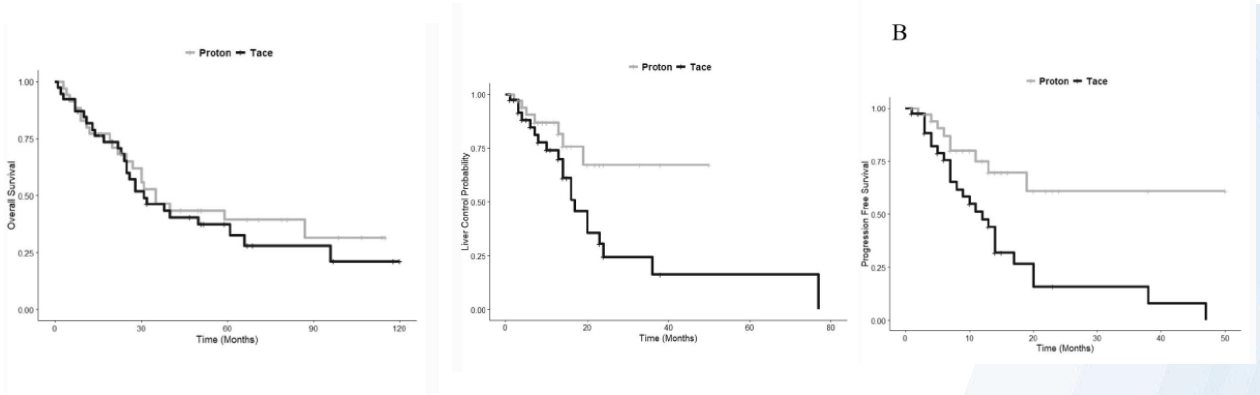



RCT
Neu diagnostiziertes, limited stage HCC

## Proton beam radiotherapy versus transarterial chemoembolization for hepatocellular carcinoma: Results of a randomized clinical trial

David A. Bush MD[1] | Michael Volk MD[2] | Jason C. Smith MD[3] | Mark E. Reeves MD, PhD[4] | Samrat Sanghvi MD[1] | Jerry D. Slater MD[1] | Michael deVera MD[2]

Cancer. 2023;1–10.




- OS vergleichbar
- LC und PFS signifikant besser mit PBT
- weniger Behandlungs-sessions
- niedrigere Toxizität (Oberbauch-Schmerzen, Nausea, Fatigue)
- weniger Krankenhaus-Aufenthalte
- weniger Kosten

TABLE 4 Hospitalizations (within 30 days) after PBT and TACE.

| | PBT ($n$ = 36) | TACE ($n$ = 39) | $p$ |
|---|---|---|---|
| Treatment courses | 43 | 69 | |
| Subjects hospitalized within 30 days of treatment | 2 | 62 | <.001 |
| Total days hospitalized, all patients | 24 | 166 | <.001 |
| Days hospitalized for routine post PBT/TACE observation | 0 | 53 | |

Abbreviations: PBT, proton beam radiotherapy; TACE, transarterial chemoembolization.

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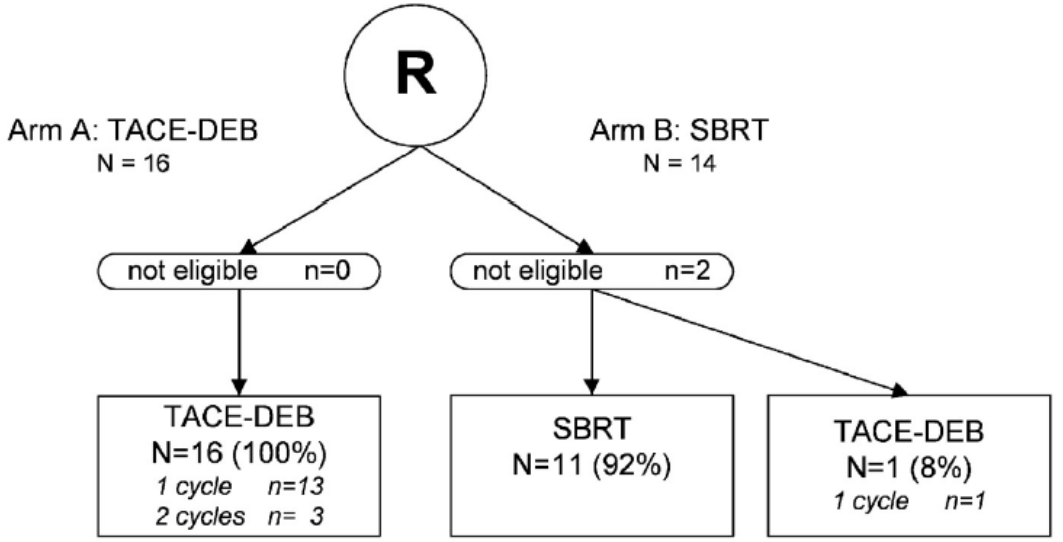
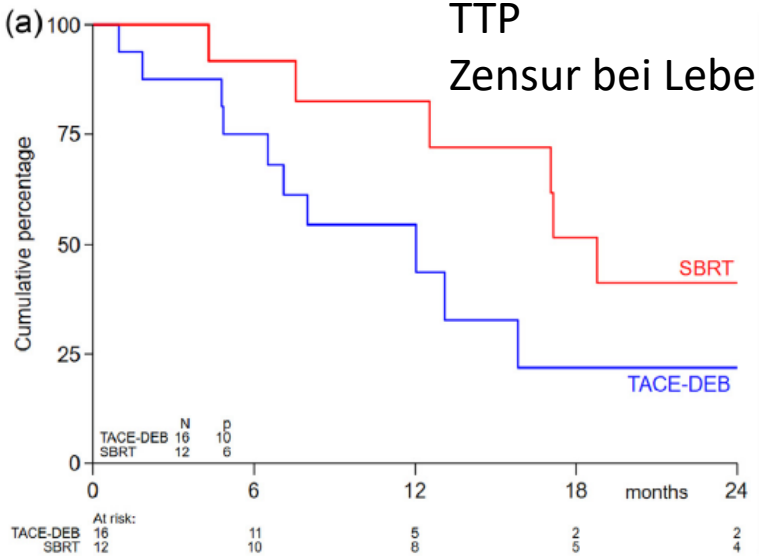
https://doi.org/10.1016/j.ijrobp.2023.03.064

# SBRT vs. TACE

## Transarterial Chemoembolization With Drug-Eluting Beads Versus Stereotactic Body Radiation Therapy for Hepatocellular Carcinoma: Outcomes From a Multicenter, Randomized, Phase 2 Trial (the TRENDY Trial)

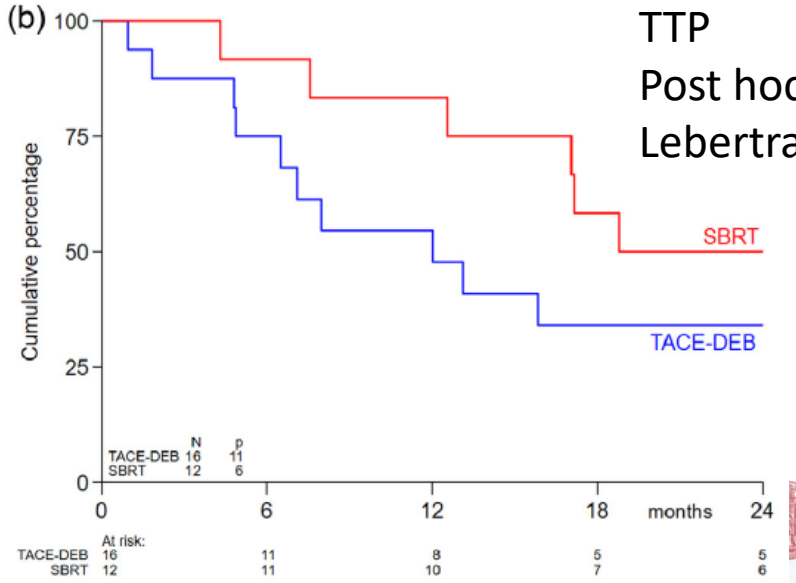
Alejandra Méndez Romero, MD, PhD,* Bronno van der Holt, PhD,* Francois E.J.A. Willemssen, MD,† Rob A. de Man, MD, PhD,‡ Ben J.M. Heijmen, PhD,* Steven Habraken, PhD,* Henrike Westerveld, MD, PhD,§ Otto M. van Delden, MD, PhD,‖ Heinz-Josef Klümpen, MD, PhD,¶ Eric T.T.L. Tjwa, MD, PhD,# Pètra M. Braam, MD, PhD,** Sjoerd F.M. Jenniskens, MD, PhD,†† Thomas Vanwolleghem, MD, PhD,‡‡ Reinhilde Weytjens, MD,§§,‖‖ Olivier d'Archambeau, MD, PhD,¶¶ Judith de Vos-Geelen, MD, PhD,## Jeroen Buijsen, MD, PhD,*** Christiaan van der Leij, MD, PhD,††† Wilhelm den Toom,* Dave Sprengers, MD, PhD,‡ Jan N.M. IJzermans, MD, PhD,‡‡‡ and Adriaan Moelker, MD, PhD†




TTP

Zensur bei Lebertransplantation




TTP

Post hoc analysis (keine Zensur bei Lebertransplantation)

Median FU 21 months

Median TTP
12. vs. 19m
p=n.s.

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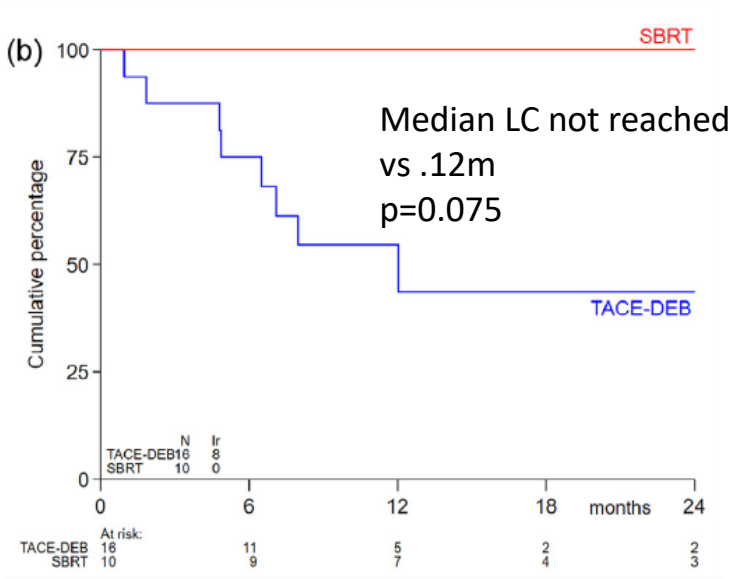
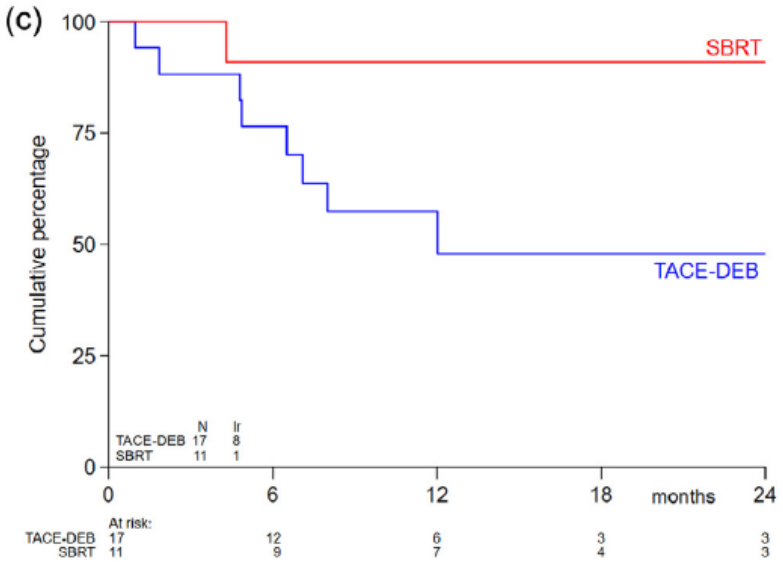
https://doi.org/10.1016/j.ijrobp.2023.03.064

## LC
## Modified intention to treat



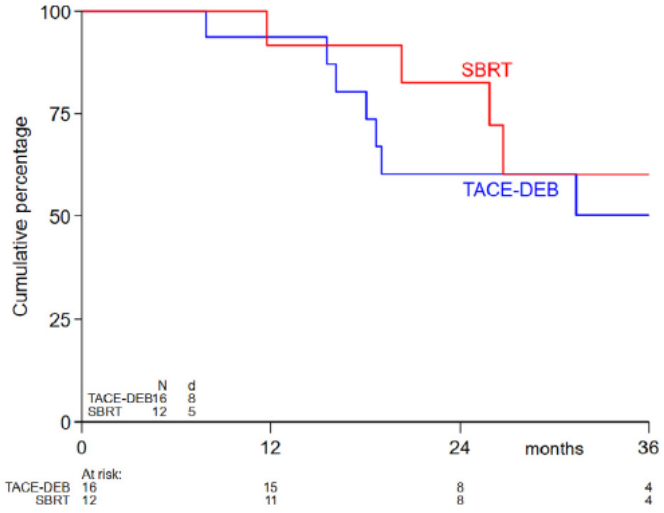

Median LC not reached
vs .12m
p=0.075

## LC
## Population as treated




## OS

Median OS 36.8m vs. 44m
p=n.s.




- SBRT mit signifikant höherer LC
- DEB-TACE mit mehr >Grade 3 Tox
- SBRT in allen Settings mit hohem lokalem Kontrollrate (90%)
- Patientenzahl zu gering (28 von geplanten 100) – eingeschränkte Statistik
- Gründe: Geringe HCC Inzidenz in Europa; Einschlusskriterien (CP A, 6cm, kein MVI, kein Aszites und keine oesophageale Varizen)
- interdisziplinäre Zusammenarbeit verbesserbar
- Jedoch: Studie etabliert hohe Qualitätskriterien in der Strahlentherapie und präsentiert eine hohe LC

**Table 2** Maximum toxicity scored in the TACE-DEB (n = 16) and in the SBRT (n = 11) safety populations after treatment

| System organ class | CTCAE grade 3 no. (%) | | CTCAE grade 4 no. (%) | | CTCAE grade 5 no. (%) | | CTCAE grades 3-5 no. (%) | |
|---|---|---|---|---|---|---|---|---|
| | TACE | SBRT | TACE | SBRT | TACE | SBRT | TACE | SBRT |
| Any AE | 4 (25) | 6 (55) | 1 (6) | 1 (9) | 1 (6) | - | 6 (38) | 7 (64) |
| Blood and lymphatic | 2 (13) | - | - | - | - | - | 2 (13) | - |
| Cardiac | - | 1 (9) | - | 1 (9) | - | - | - | 2 (18) |
| Gastrointestinal | 1 (6) | - | - | 1 (9) | - | - | 1 (6) | 1 (9) |
| Hepatobiliary | 1 (6) | - | - | - | - | - | 1 (6) | - |
| Infections/infestations | 1 (6) | 2 (18) | 1 (6) | - | - | - | 2 (13) | 2 (18) |
| Procedure complications | 1 (6) | 1 (9) | - | - | - | - | 1 (6) | 1 (9) |
| Investigations | 2 (13) | 2 (18) | - | - | - | - | 2 (13) | 2 (18) |
| Metabolism and nutrition | 2 (13) | - | - | - | - | - | 2 (13) | - |
| Nervous system | - | 1 (9) | - | - | 1 (6) | - | 1 (6) | 1 (9) |
| Renal and urinary | 1 (6) | - | - | - | - | - | 1 (6) | - |
| Respiratory/thoracic/ Mediastinal | 1 (6) | 1 (9) | - | - | - | - | 1 (6) | 1 (9) |

The maximum follow-up considered for the table was 2 years.
*Abbreviations:* AE = adverse event; CTCAE = Common Terminology Criteria for Adverse Events; SBRT = stereotactioc body radiation therapy; TACE-DEB = transarterial chemoembolization delivered with drug eluting beads.

**Therapieentscheidungen beim hepatozellulären Karzinom: Erkenntnisse aus der TRENDY-Studie**

Strahlentherapie und Onkologie
https://doi.org/10.1007/s00066-023-02140-3

Danny Jazmati[1,4] · Judit Boda-Heggemann[2] · Oliver Blanck[3] · David Krug[3]

dkfz. DEUTSCHES KREBSFORSCHUNGSZEN IN DER HELMHOLTZ-GEMEIN

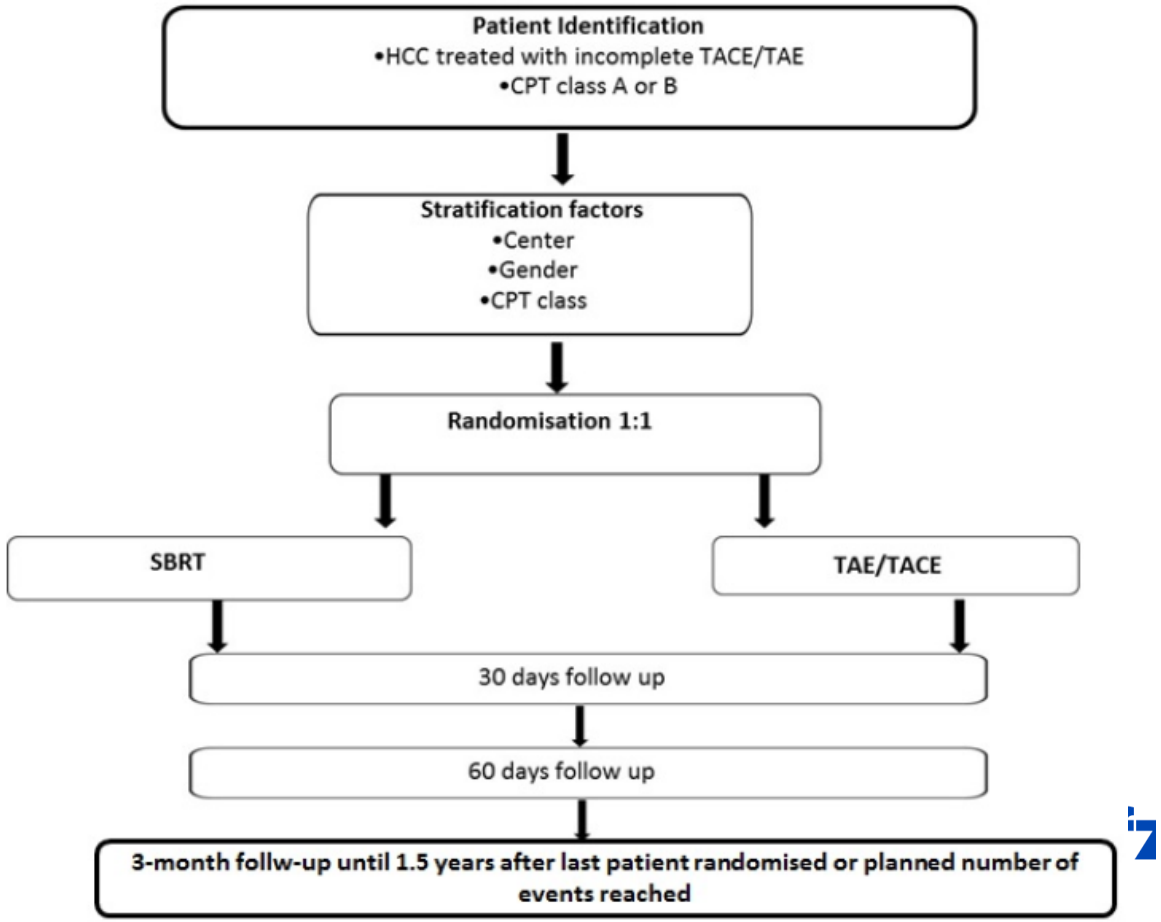
# Kombination?

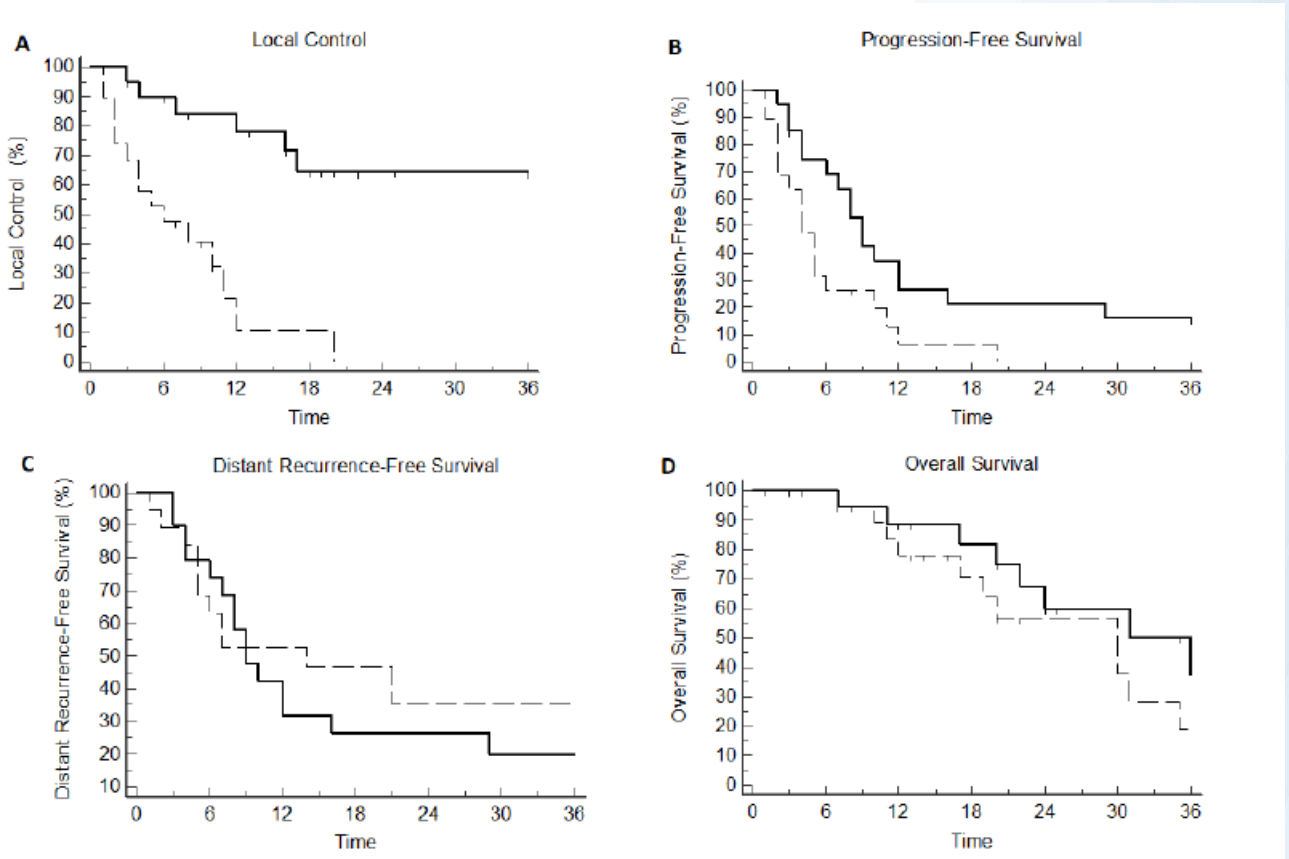
*Curr. Oncol.* **2022**, *29*

**Stereotactic Radiotherapy after Incomplete Transarterial (Chemo-) Embolization (TAE\TACE) versus Exclusive TAE or TACE for Treatment of Inoperable HCC: A Phase III Trial (NCT02323360)**

Tiziana Comito [1], Mauro Loi [2], Ciro Franzese [1,3], Elena Clerici [1], Davide Franceschini [1,*], Marco Badalamenti [1], Maria Ausilia Teriaca [1], Lorenza Rimassa [3,4], Vittorio Pedicini [5], Dario Poretti [5], Luigi Alessandro Solbiati [3,5], Guido Torzilli [3,6], Roberto Ceriani [7], Ana Lleo [3,7], Alessio Aghemo [3,7], Armando Santoro [3,4] and Marta Scorsetti [1,3]

- Ph III
- Inop HCC, incompl. response nach >1 TAE/TACE
- SBRT höhere LC als wiederholte TAE/TACE
- SBRT: bessere PFS
- Kein OS Benefit



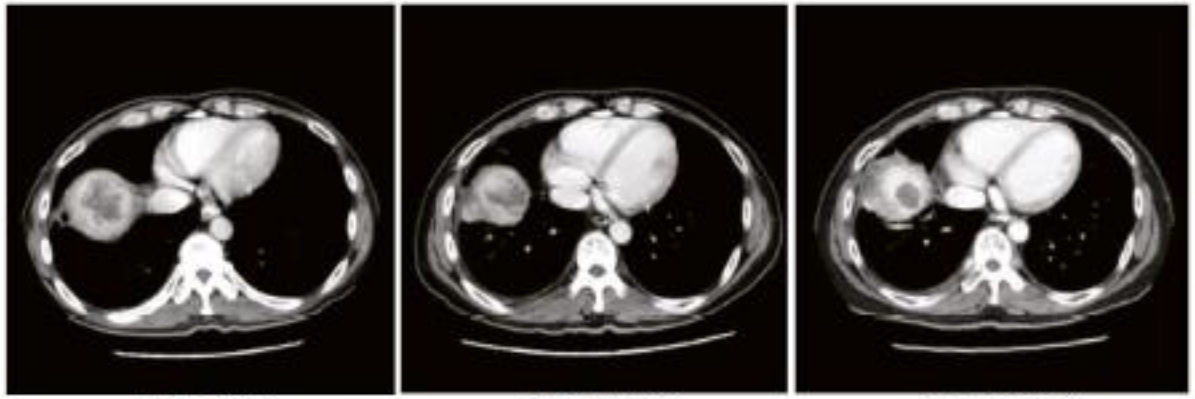



HEPATOLOGY
HEPATOLOGY, VOL. 74, NO. 5, 2021

# Prospective Study of Stereotactic Body Radiation Therapy for Hepatocellular Carcinoma on Waitlist for Liver Transplant

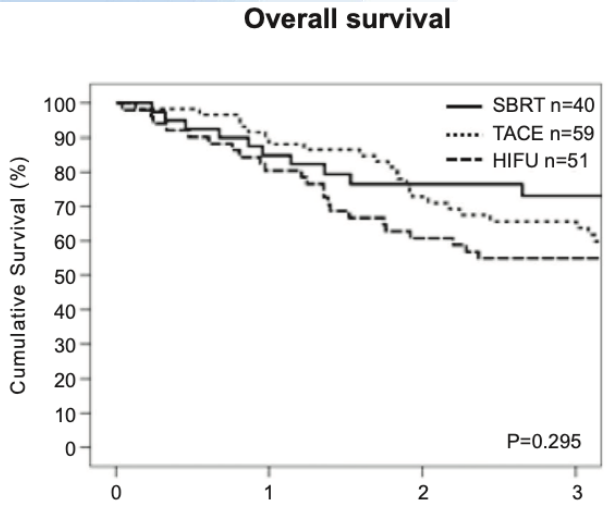
Tiffany Cho-Lam Wong [1,2] Victor Ho-Fun Lee,[3,4] Ada Lai-Yau Law,[5] Herbert H. Pang,[6] Ka-On Lam,[3,4] Vince Lau,[7] Tracy Yushi Cui,[2] Adrianna Sze-Yin Fong [1] Sarah Wai-Man Lee,[5] Edwin Chun-Yin Wong,[5] Jeff Wing-Chiu Dai,[1,2] Albert Chi-Yan Chan,[1,2] Tan-To Cheung,[1,2] James Yan-Yue Fung [8,9] Rebecca Met-Wan Yeung,[5] Mai-Yee Luk,[3,4] To-Wai Leung [3,4] and Chung-Mau Lo[1,2]

B



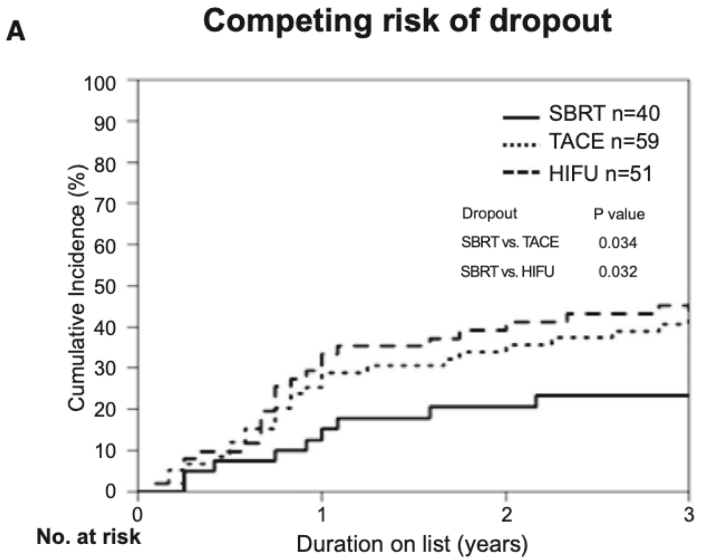

Explant showed complete pathological necrosis

From the time of listing




| No at risk | | | | |
|---|---|---|---|---|
| SBRT | 40 | 32.5 | 24 | 21 |
| TACE | 59 | 52 | 41.5 | 34 |
| HIFU | 51 | 41 | 31 | 28 |

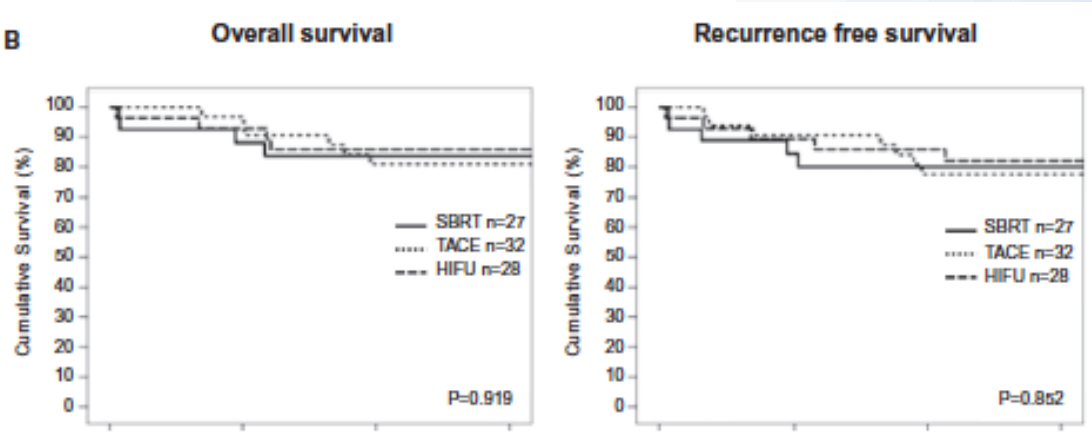
A




| No. at risk | | | | |
|---|---|---|---|---|
| SBRT | 40 | 30 | 22 | 19 |
| TACE | 59 | 42 | 33 | 28 |
| HIFU | 51 | 34 | 26 | 24 |

From the time of transplant

B




| No at risk | | | | |
|---|---|---|---|---|
| SBRT | 27 | 20 | 19 | 15 |
| TACE | 32 | 31 | 25 | 24 |
| HIFU | 28 | 26 | 24 | 24 |

| No at risk | | | | |
|---|---|---|---|---|
| SBRT | 27 | 19 | 18 | 14 |
| TACE | 32 | 29 | 24 | 23 |
| HIFU | 28 | 25 | 24 | 23 |

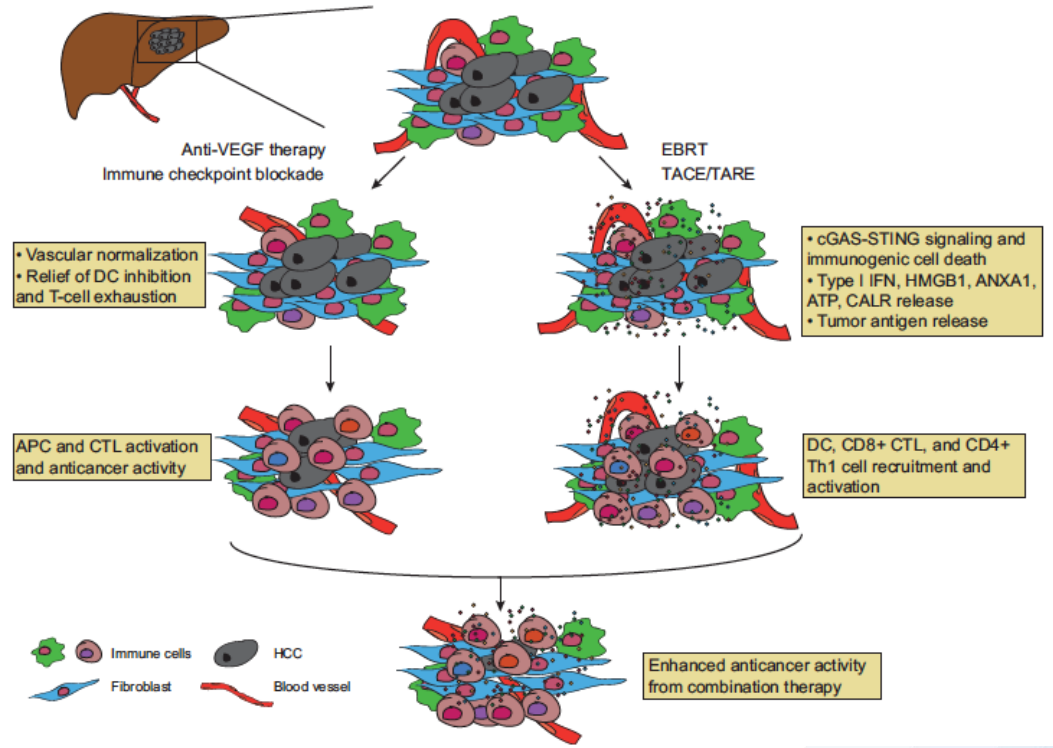
# Integration of Systemic and Liver-Directed Therapies for Locally Advanced Hepatocellular Cancer: Harnessing Potential Synergy for New Therapeutic Horizons

Eric H. Bent, MD, PhD[1]; Eric Wehrenberg-Klee, MD[2]; Eugene J. Koay, MD, PhD[3]; Lipika Goyal, MD[4,*]; and Jennifer Y. Wo, MD[1,*]

**Table 1. Ongoing Prospective Trials Combining RT and Systemic Therapies**

| Trial | Study Type | N (Anticipated) | ClinicalTrials.gov Identifier | Agent Class |
|---|---|---|---|---|
| RTOG1112: sorafenib ± SBRT | Randomized phase III | 368 | NCT01730937 | Anti–VEGF TKI |
| Sorafenib ± TACE + SBRT | Randomized phase III | 54 | NCT04387695 | Anti–VEGF TKI |
| Sorafenib ± proton RT | Randomized outcomes trial | 220 | NCT01141478 | Anti–VEGF TKI |
| Sorafenib + RT + HAIC (5-FU) | Single-arm phase II | 47 | NCT02425605 | Anti–VEGF TKI |
| Sorafenib + RT | Single-arm phase II | 86 | NCT03535259 | Anti–VEGF TKI |
| Sorafenib + RT | Single-arm phase II | 45 | NCT01328223 | Anti–VEGF TKI |
| Axitinib vs RT vs RT + axitinib | Randomized phase II 2 × 2 | 160 | NCT03732105 | Anti–VEGF TKI |
| Apatinib ± RT | Randomized phase II | 50 | NCT03520257 | Anti–VEGF TKI |
| Axitinib + RT | Phase I | 9 | NCT02814461 | Anti–VEGF TKI |
| SBRT ± sintilimab | Randomized phase II/III | 116 | NCT04167293 | Anti–PD-1/PD-L1 |
| Sintilimab ± SBRT | Randomized phase II | 84 | NCT04547452 | Anti–PD-1/PD-L1 |
| Durvalumab + tremelimumab + SBRT | Single-arm phase II | 70 | NCT03482102 | Anti–PD-1/PD-L1 |
| Carrelizumab + SBRT | Single-arm phase II | 39 | NCT04193696 | Anti–PD-1/PD-L1 |
| START-FIT: avelumab + TACE + SBRT | Single-arm phase II | 33 | NCT03817736 | Anti–PD-1/PD-L1 |
| PEMRAD: pembrolizumab + SBRT | Single-arm phase II | 30 | NCT03316872 | Anti–PD-1/PD-L1 |
| IBI308 (anti–PD-1) + SBRT | Single-arm phase II | 30 | NCT03857815 | Anti–PD-1/PD-L1 |
| Toripalimab + SBRT | Single-arm phase II | 30 | NCT04169399 | Anti–PD-1/PD-L1 |
| Durvalumab + SBRT ± tremelimumab | Single-arm phase II | 30 | NCT04430452 | Anti–PD-1/PD-L1 |
| Nivolumab + SBRT ± ipilimumab | Phase I | 50 | NCT03203304 | Anti–PD-1/PD-L1 |
| Sintilimab (anti–PD-1) + SBRT | Phase I | 20 | NCT04104074 | Anti–PD-1/PD-L1 |
| Carrelizumab + apatinib + SBRT | Single-arm phase II | 27 | NCT04523662 | Anti–PD-1/PD-L1 |
| Neoantigen T-cell infusion + RT | Single-arm phase I/II | 40 | NCT03199807 | Cell therapy |
| Dendritic cell infusion + PCV13 + RT | Phase I | 26 | NCT03942328 | Cell therapy |
| CAPOX + RT | Phase I | 30 | NCT02403544 | Chemotherapy |
| Endostatin + RT | Single-arm phase II | 61 | NCT03208335 | Anti-VEGF |
| Galunisertib + RT | Phase I | 15 | NCT02906397 | Anti–TGF-$\beta$ |

Abbreviations: CAPOX, capecitabine/oxaliplatin; HAIC, hepatic arterial infusion chemotherapy; PCV13, pneumococcal 13-valent conjugate vaccine; RT, radiation therapy; SBRT, stereotactic body radiation therapy; TACE, transarterial chemoembolization; TGF-$\beta$, transforming growth factor $\beta$; TKI, tyrosine kinase inhibitor; VEGF, vascular endothelial growth factor.




NOT YET RECRUITING

**Phase Ib/II Trial of Combining Pembrolizumab and Lenvatinib With SBRT for HCC Patients With Portal Vein Thrombosis.**

ClinicalTrials.gov ID NCT05286320
Sponsor National Taiwan University Hospital
Information provided by National Taiwan University Hospital (Responsible Party)
Last Update Posted 2023-03-02

UNKNOWN STATUS

**Combination of Sintilimab and Stereotactic Body Radiotherapy in Hepatocellular Carcinoma (ISBRT01) (ISBRT01)**

ClinicalTrials.gov ID NCT04167293
Sponsor Mian XI
Information provided by Mian XI, Sun Yat-sen University (Responsible Party)
Last Update Posted 2021-03-23

UMM UNIVERSITÄTSMEDIZIN MANNHEIM

DKFZ -Hector Krebsinstitut

dkfz. DE KR IN I

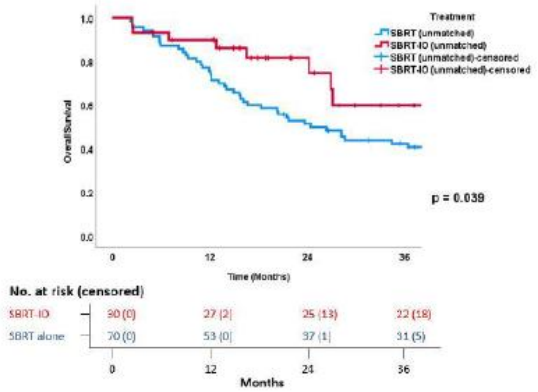
UNIVERSITÄT HEIDELBERG ZUKUNFT SEIT 1386

# Survival Outcome Analysis of Stereotactic Body Radiotherapy and Immunotherapy (SBRT-IO) versus SBRT-alone in Unresectable Hepatocellular Carcinoma (HCC)

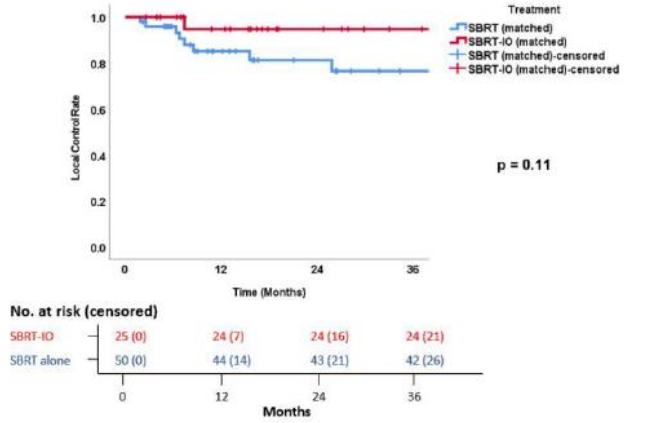
Liver Cancer , DOI: 10.1159/000533425

Chiang CL, Lee FAS, Chan KSK, Lee VWY, Chiu KWH, Ho RLM, Fong JKS, Wong NSM, Yip WWL, Yeung CSY, Lau VWH, Kwan M, Kong F-MS, Chan ACY

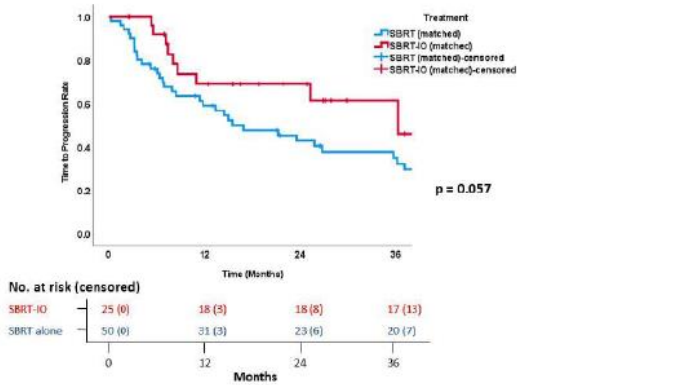
| | SBRT-IO (n=30) | SBRT (n=70) | P value |
|---|---|---|---|
| 12-month rate, % | 89.9% (72.0% – 96.6%) | 75.7% (63.9% – 84.1%) | 0.039 |
| 24-month rate, % | 81.6% (61.1% – 92.0%) | 51.3% (39.0% – 62.3%) | |
| 36-month rate, % | 59.8% (32.9% – 78.8%) | 42.3% (30.5% – 53.6%) | |
| Median, months | NR (2.5 – 59.6 months) | 24.5 months (2.2 – 69.9 months) | |



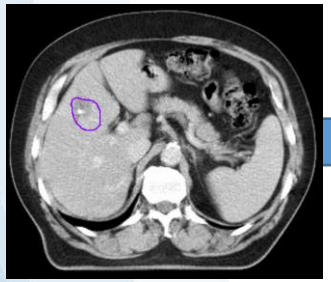

| | SBRT-IO (n=25) | SBRT (n=50) | P value |
|---|---|---|---|
| 12-month rate, % | 94.7% (68.5% – 99.2%) | 85.2% (69.5% – 93.2%) | 0.11 |
| 24-month rate, % | 94.7% (68.5% – 99.2%) | 81.3% (64.0% – 90.8%) | |
| 36-month rate, % | 94.7% (68.5% – 99.2%) | 76.5% (57.2% – 88.0%) | |




| | SBRT-IO (n=25) | SBRT (n=50) | P value |
|---|---|---|---|
| 12-month rate, % | 68.9% (45.5% – 83.8%) | 58.9% (43.7% – 71.3%) | 0.057 |
| 24-month rate, % | 68.9% (45.5% – 83.8%) | 40.5% (26.3% – 54.3%) | |
| 36-month rate, % | 61.3% (35.9% – 79.1%) | 32.5% (19.1% – 46.6%) | |
| Median, months | 30.8 months (2.6 – 59.6 months) | 15.0 months (0.3 – 69.9 months) | |

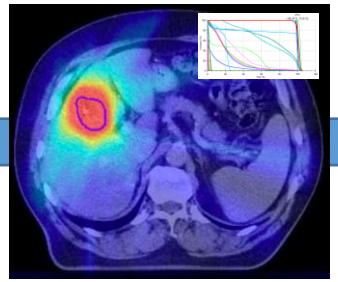


# Ausblick: Adaptive RT



Planungs-CT

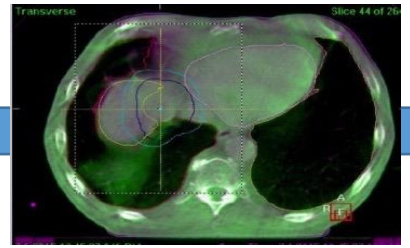
Konturierung



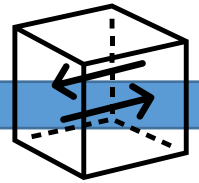
Inverse Planung

Dosisberechnung

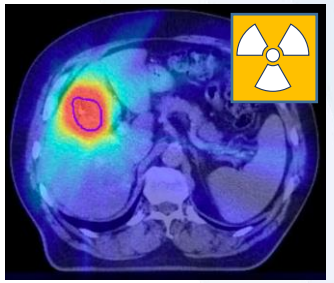
QA




CBCT

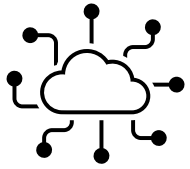


Verschiebung

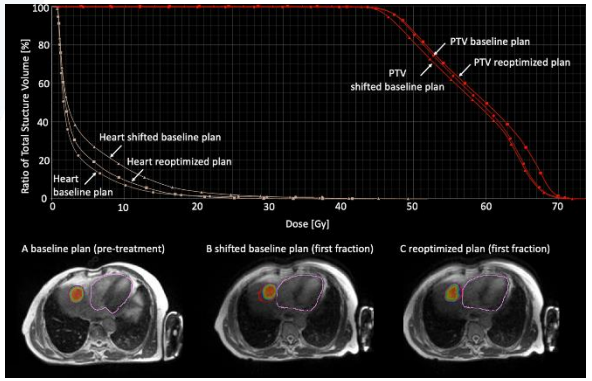


Bestrahlung

Adaptive Umplanung



Automatisiert:
Tägliche
Online
Adaptation
($\Delta$ t ≈ 15 min)




*Mayinger M et al., Radiat Oncol. 2021 May 4;16(1):84.*

1. Hochqualitative Bildgebung
2. Künstliche Intelligenz: Bestrahlungsplanung

DEGRO
ARBEITSGRUPPE RADIOCHIRURGIE/ STEREOTAXIE

Hep Reg

UKD Universitätsklinikum Düsseldorf

***Real-world data on patients treated with stereotactic body radiotherapy (SBRT) for Hepatocellular Carcinoma (HCC) (HepReg)***

**AN INTERNATIONAL MULTICENTRE REGISTRY COLLECTING DATA ON PATIENTS TREATED WITH SBRT FOR HCC ( HepReg)**

# HepReg

Projektleitung: Dr. Danny Jazmaty, Düsseldorf/ Prof. Dr. Thomas Brunner, Graz
Involvierte Kliniken: Kiel, Mannheim, Freiburg, Essen…

UMM UNIVERSITÄTSMEDIZIN MANNHEIM

DKFZ -Hector Krebsinstitut

dkfz. DEUTSCHES KREBSFORSCHUNGSZENTRUM IN DER HELMHOLTZ-GEMEINSCHAFT

Medizinische Fakultät Mannheim der Universität Heidelberg
Universitätsklinikum Mannheim

UNIVERSITÄT HEIDELBERG ZUKUNFT SEIT 1386

# Zusammenfassung

**AASLD Practice Guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma**

Amit G. Singal[1] | Josep M. Llovet[2,3,4] | Mark Yarchoan[5] | Neil Mehta[6] | Julie K. Heimbach[7] | Laura A. Dawson[8] | Janice H. Jou[9] | Laura M. Kulik[10] | Vatche G. Agopian[11] | Jorge A. Marrero[12] | Mishal Mendiratta-Lala[13] | Daniel B. Brown[14] | William S. Rilling[15] | Lipika Goyal[16] | Alice C. Wei[17] | Tamar H. Taddei[18,19]

Clinical consensus statement: Establishing the roles of locoregional and systemic therapies for the treatment of intermediate-stage hepatocellular carcinoma in Canada

Jason K. Wong[a,*], Howard J. Lim[b], Vincent C. Tam[c], Kelly W. Burak[d], Laura A. Dawson[e], Prosanto Chaudhury[f], Robert J. Abraham[g], Brandon M. Meyers[h], Gonzalo Sapisochin[i], David Valenti[j], Setareh Samimi[k], Ravi Ramjeesingh[l], Amol Mujoomdar[m], Ilidio Martins[n], Elijah Dixon[o], Maja Segedi[p], David M. Liu[q]

Cancer Treatment Reviews 115 (2023) 102526

- Palliative RT bei Schmerzen indiziert und hochwirksam (CCTG HE.1 )
- Oligometastasierte Situation: lokale Therapie von Oligomets kann angeboten werden
- Lokale RT in Kombination mit Systemtherapie mit Benefit (RTOG 1112), Rolle mit aktuellen Systemtherapien wird in prosp. Studien untersucht
- SBRT/PBT im Vergleich mit TACE und RFA sicher und effektiv, viele abgebrochene Studien, Kombinationstherapie vielversprechend
- Bridge vor Transplantation:  SBRT sicher und effektiv
- SBRT insbesondere für große Tumore (>4cm)/Rezidive/ mit Gefäßinfiltration/technisch schwer machbaren Thermoablation eine sinnvolle Alternative

# Danke für Ihre Aufmerksamkeit!

- DEGRO AG SBRT
  - Team Leber: Prof Gkika, Prof. Corradini, Dr. Gerum, Dr. Jazmaty
  - HEPReg: Dr. Jazmaty
- DGMP AG SBRT, Dr. Blanck
- UMM Team Leber: PD Dr. Dreher, Dr. Kästner, Prof Dr. Bürgy, Prof. Giordano/ Prof. A. Teufel
- Strahlentherapie-Team HCC S3-LL:
  - Prof. Brunner
  - Prof. Gkika
  - PD Dr. Krug