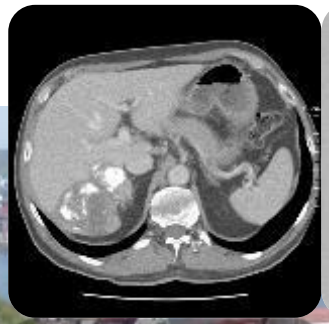
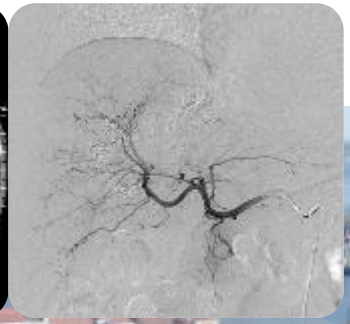
DFIR 7th and 8th October 2021

Dansk Forening for Interventionel Radiologi / Danish Society of Interventional Radiology

TACE: New concepts and paradigms





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Dept. of Diagnostic and Interventional Radiology / Neuroradiology

Disclosure

Speaker name:

.....Silke Hopf-Jensen.....

I have the following potential conflicts of interest to report:

- [x] speaker honoraria: Terumo
- [ ] Employment in industry
- [ ] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [ ] Other(s)

- [ ] I do not have any potential conflict of interest

Objectives

I. History and Indications

II. TACE techniques

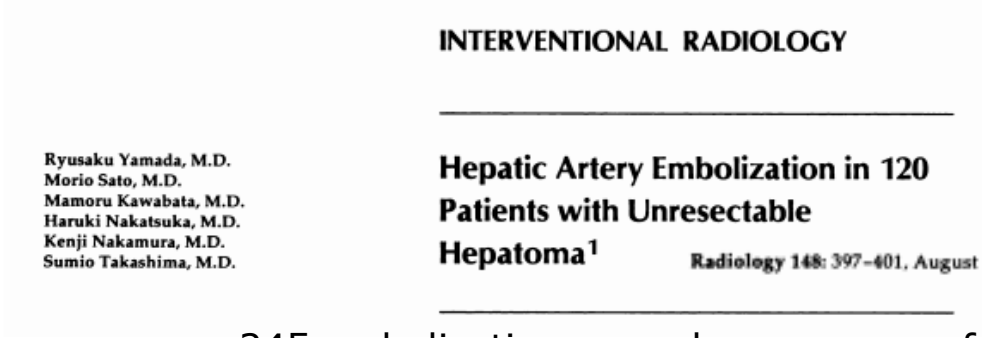
III. Outcome and Follow-up

IV. Future perspectives

I. History and Indications

Yamada R, Nakatsuka H, Nakamura K, et al. (1979) [Super-selective arterial embolization in unresectable hepatomas Nihon Igaku Hoshasen Gakkai zasshi. Nippon acta radiologica, 39(5):540-543

First evidence for TACE being published by Yamada et al in 1979



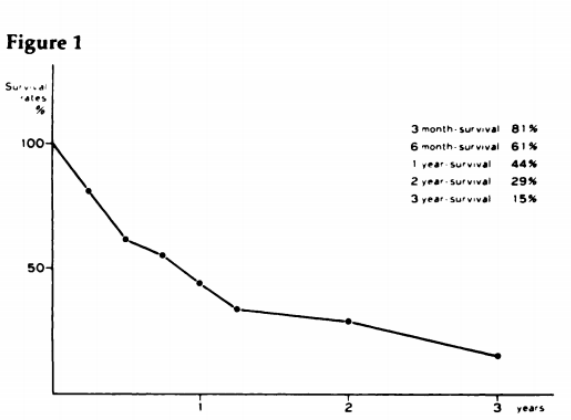
INTERVENTIONAL RADIOLOGY

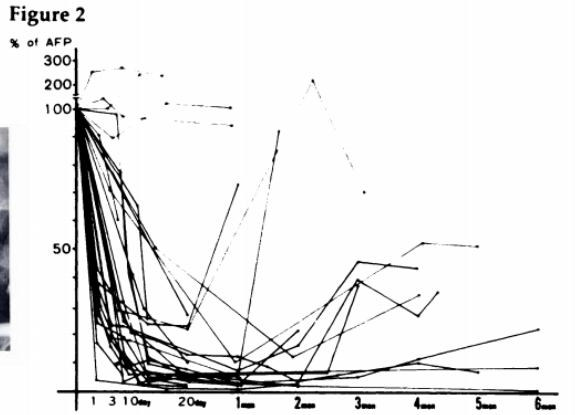
Ryusaku Yamada, M.D.
Morio Sato, M.D.
Mamoru Kawabata, M.D.
Haruki Nakatsuka, M.D.
Kenji Nakamura, M.D.
Sumio Takashima, M.D.

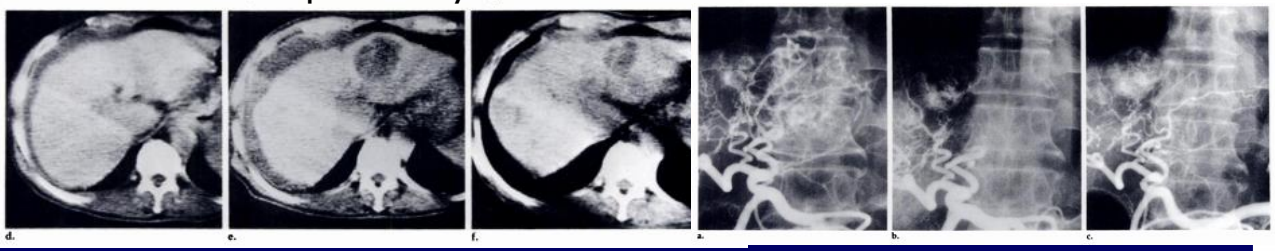
Hepatic Artery Embolization in 120 Patients with Unresectable Hepatoma[1]

Radiology 148: 397–401, August 1983

- 245 embolization procedures were performed in 120 patients with unresectable hepatoma.
- A gelatin sponge pieces were permeated with 10 mg of mitomycin C or 20 mg of adriamycin and contrast material.
- The AFP value in 90% of these cases decreased remarkably immediately after embolization.
- The 1-year, 2-year, and 3-year cumulative survival rates were 44%, 29%, and 15%, respectively.



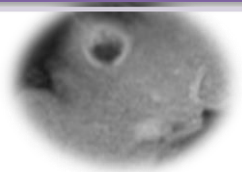




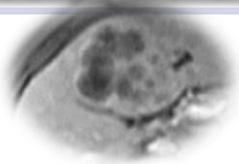
I. Indications

- primary and secondary liver tumours
- HCC and ICC account for 9.1% of all cancer deaths worldwide.
- Half of all patients with CRC develop liver metastases during the course of the disease.
- The liver is also the most common site of metastases from NET.

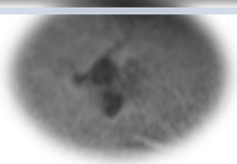
HCC
hepatocellular carcinoma



ICC
intrahepatic cholangiocarcinoma



mCRC
metastases from colorectal cancer



NET
neuroendocrine tumours

I. Indications

Vogel A, Cervantes A, Chau I, et al. (2018) Hepatocellular carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†. Annals of Oncology, 29(Supplement_4):iv238iv255

therapy decision is made by a multidisciplinary tumour board, which includes hepatologists, oncologists, surgeons, diagnostic and interventional radiologists

HCC
hepatocellular carcinoma

- Barcelona Clinic Liver Cancer (BCLC) recommondation: Stages 0-A, Stage B, in the transplant setting with a class of recommendation of IB and IA

DOWN-STAGING
BRIDGING
PALLIATIVE

ICC
intrahepatic cholangiocarcinoma

- surgically unresectable or inoperable liver tumours with liver-only or liver-dominant disease

mCRC
metastases from colorectal cancer

- liver-limited disease in whom the available chemotherapeutic lines have failed

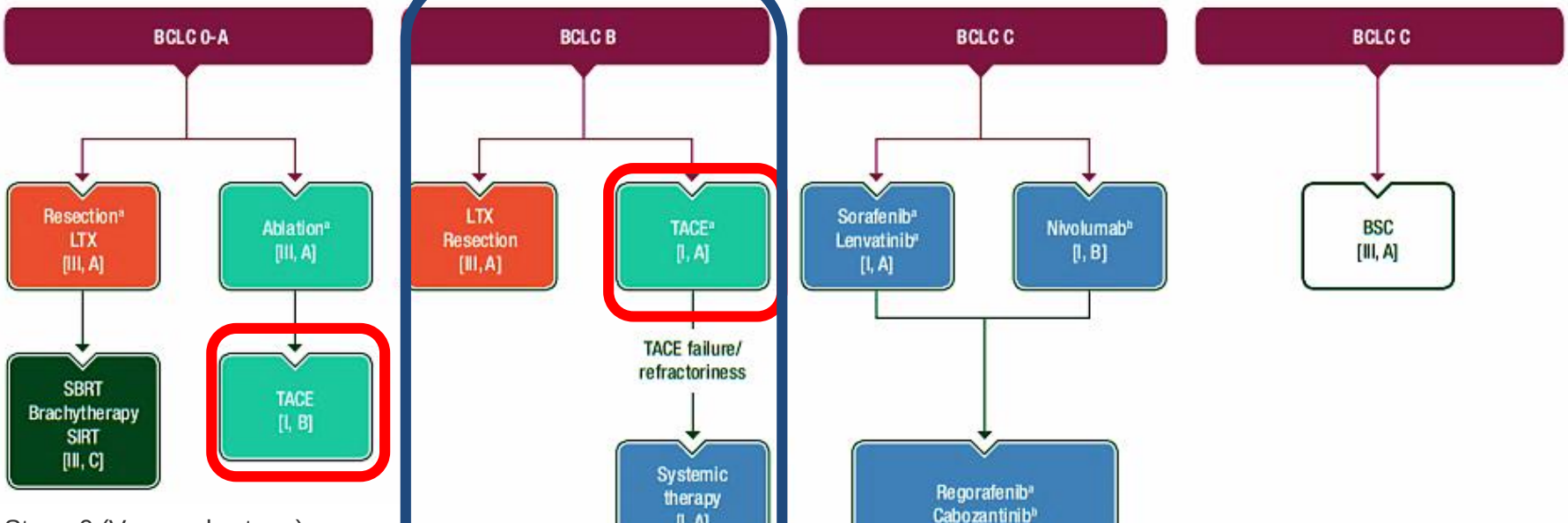
NET
neuroendocrine tumours

- alternative therapy to surgical resection of liver metastasis
- alternative to systemic treatment in those patients with NETs with disease limited to the liver

I. Indications HCC

Kudo, M.; Han, K.H. et al. A changing paradigm for the treatment of intermediate-stage hepatocellular carcinoma: Asia-Pacific Primary Liver Cancer Expert Consensus Statements. Liver Cancer 2020, 9, 245–260.

European Society of Medical Oncology (ESMO) guidelines on HCC 2020



Stage 0 (Very early stage)
This means the tumour is less than 2cm, you feel well (PS 0) and your liver is working normally (Child-Pugh A).

Stage A (Early stage)
This means there is a single tumour of any size, or up to 3 tumours all less than 3 cm. You feel well and are active (PS 0), and your liver is working well (Child-Pugh A or B).

Stage B (Intermediate Stage)
This means there are many tumours in the liver, but you feel well (PS 0) and your liver is working well (Child-Pugh A or B).

I. Contraindications

Gaba RC, Lokken RP, Hickey RM, et al. (2017) Quality Improvement Guidelines for Transarterial Chemoembolization and Embolization of Hepatic Malignancy. JVIR, 28(9):1210-1223 e1213

Relative contraindications

- TIPS
- segmental or subsegmental non-neoplastic portal vein thrombosis (could safely be performed if superselective).
- patients with tumour burden >50% of liver volume are unlikely to benefit from treatment.

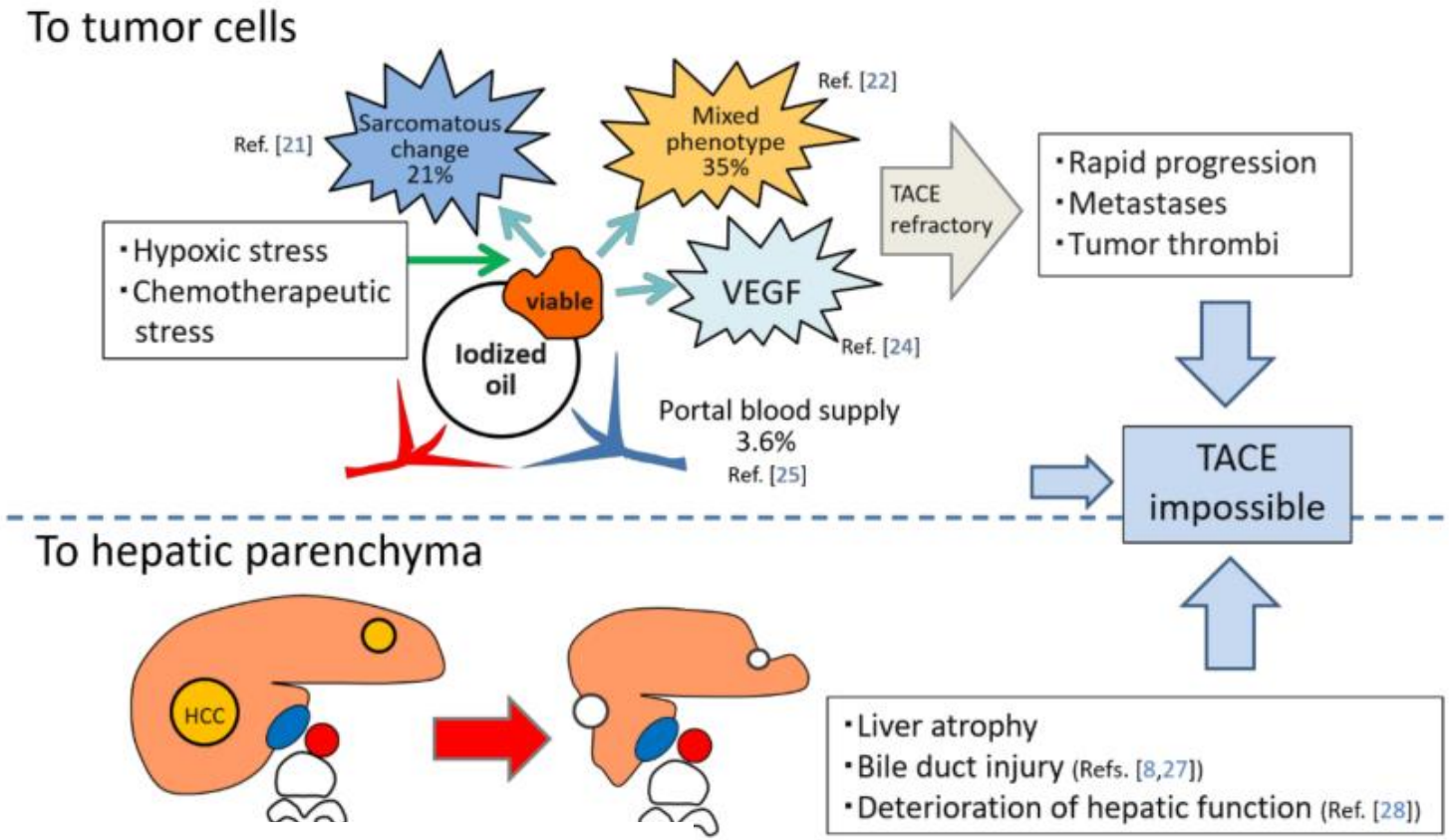
Absolute contraindications

- portal vein neoplastic thrombosis or hepatofugal blood flow
- impaired hepatic function (Child-Pugh B8 or greater)
- poor performance status (ECOG P2 or greater),
- contraindication for arteriography (uncorrectable thrombocytopenia, coagulopathy, severe renal insufficiency or severe reaction to contrast media)

I. Contraindications

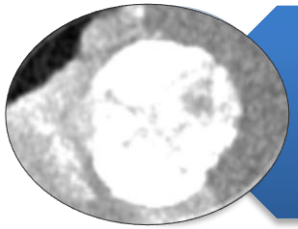
Schematic representation of negative aspects of TACE

Treatment Strategy of Transarterial Chemoembolization for Hepatocellular Carcinoma Shiro MiyayamaAppl. Sci. 2020, 10, 7337;

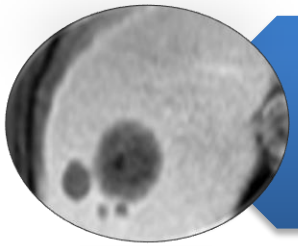


VEGF: vascular endothelial growth factor

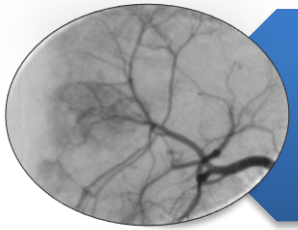
II. TACE techniques



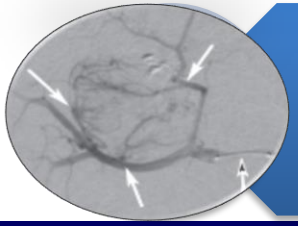
conventional TACE
(c-TACE)



drug-eluting microspheres (DEM-TACE)



Degradable Starch Microsphere (DSM-TACE)



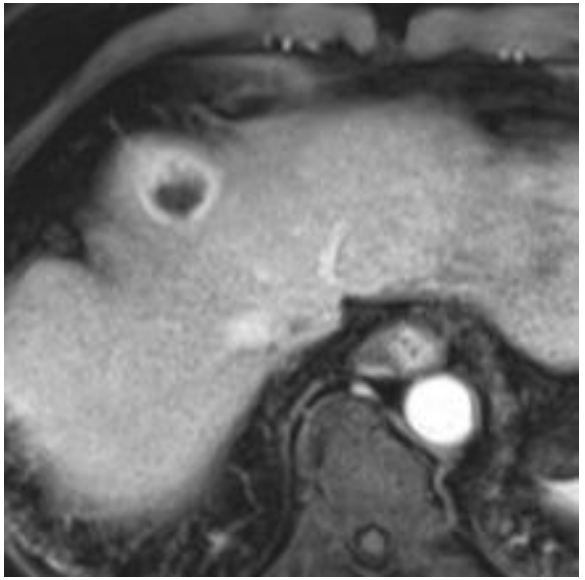
balloon-occluded TACE (b-TACE)

There is no standard technique regarding all aspects of the procedure including drugs, embolic materials, and micro-catheter selection

II. TACE techniques
Vascular access to diagnostic angiography and CBCT

- According to international guidelines, *multi-detector computed tomography (MDCT)/ magnetic resonance imaging (MRI)* is capable of establishing the diagnosis of HCC in cirrhotic patients in lesions greater than 10 mm.
- Vascular anatomy
- Size, numbers of lesions (single vs multifocal; uni-lobar vs bilobar), percentage volume of tumour spread
- Presence and extension of portal vein thombosis
- In most other tumours (mCRC, ICC, NET), *confirmatory biopsy* is usually preferred before planning a TACE session

Mitchell DG, Bruix J, Sherman M, Sirlin CB (2015) LI-RADS (Liver Imaging Reporting and Data System): Summary, discussion, and consensus of the LI-RADS Management Working Group and future directions. Hepatology, 61(3):1056-1065



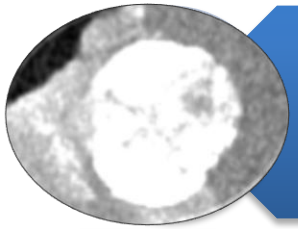
II. TACE techniques
Vascular access to diagnostic angiography and CBCT

- Detailed knowledge on the normal and variant anatomy of the visceral and hepatic arterial anatomy
- familiarity with suitable catheters and guidewires, liquid and particulate embolic agents and applicable chemotherapeutics is vital.

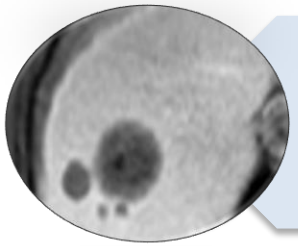
CBCT (cone beam CT):

- tumour and tumour feeder detection, detection of occult nodules.
- Useful for hypo-vascular lesions (mCRC and ICC).

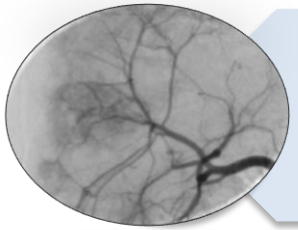
II. TACE techniques
DEM-TACE (DEB-TACE)



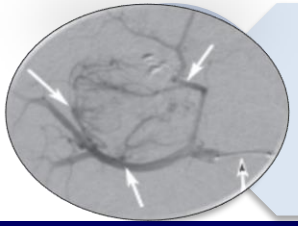
conventional TACE
(c-TACE)



drug-eluting microspheres (DEM-TACE, DEB-TACE)

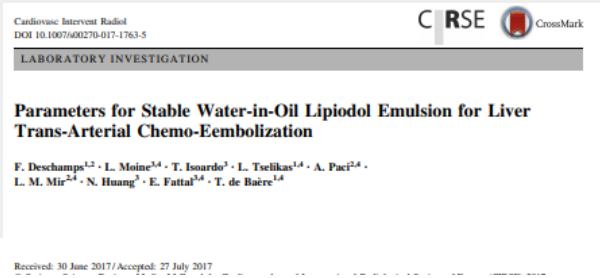


Degradable Starch Microsphere (DSM-TACE)



balloon-occluded TACE (b-TACE)

II. TACE techniques: c-TACE


Cardiovasc Intervent Radiol
DOI 10.1007/s00270-017-1763-5

CIRSE CrossMark

LABORATORY INVESTIGATION

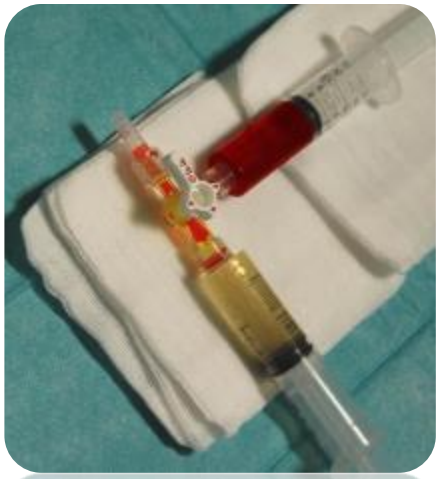
Parameters for Stable Water-in-Oil Lipiodol Emulsion for Liver Trans-Arterial Chemo-Eembolization

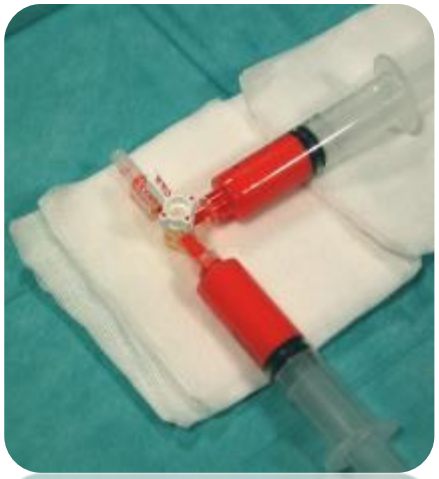
F. Deschamps[1,2] · L. Moine[3,4] · T. Isoardo[3] · L. Tselikas[1,4] · A. Paci[2,4] · L. M. Mir[2,4] · N. Huang[3] · E. Fattal[3,4] · T. de Baère[1,4]

Received: 30 June 2017 / Accepted: 27 July 2017

Embolisation

- Lipiodol (Guerbet, France) is an ethyl ester of iodized fatty acids of poppy seed oil.
- intra-arterial injection of a mixture of lipiodol and one of several anticancer drug(s), followed by the administration of an embolic agent.
- the volume of lipiodol should be greater than the volume of drug (ideally a 2:1 or 3:1)



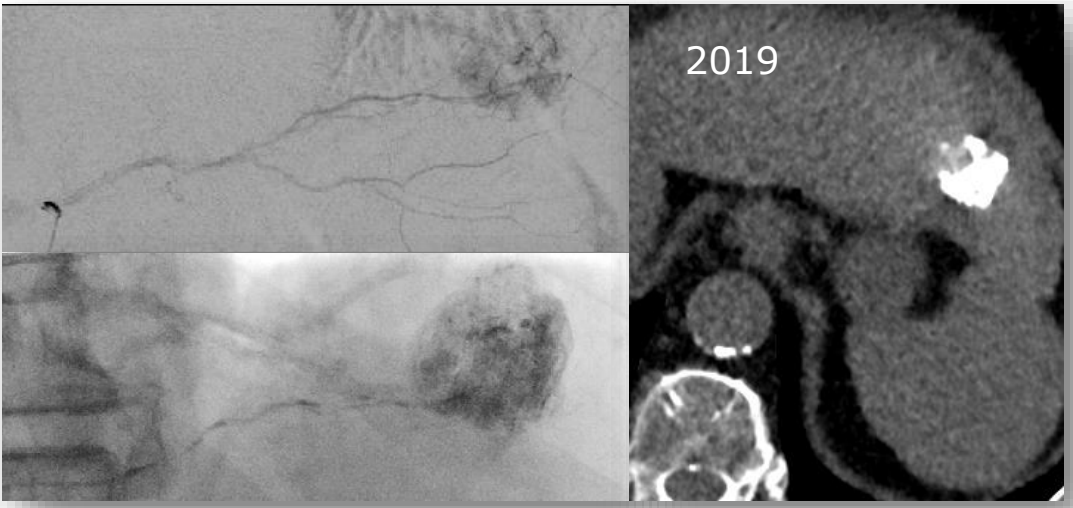


The percentage of water-in-oil emulsions (injections of doxorubicin in the Lipiodol) obtained was significantly higher for incremental (94%) and for continuous (100%) injections compared to bolus injection (6%) of doxorubicin.

II. TACE techniques: c-TACE

Embolisation

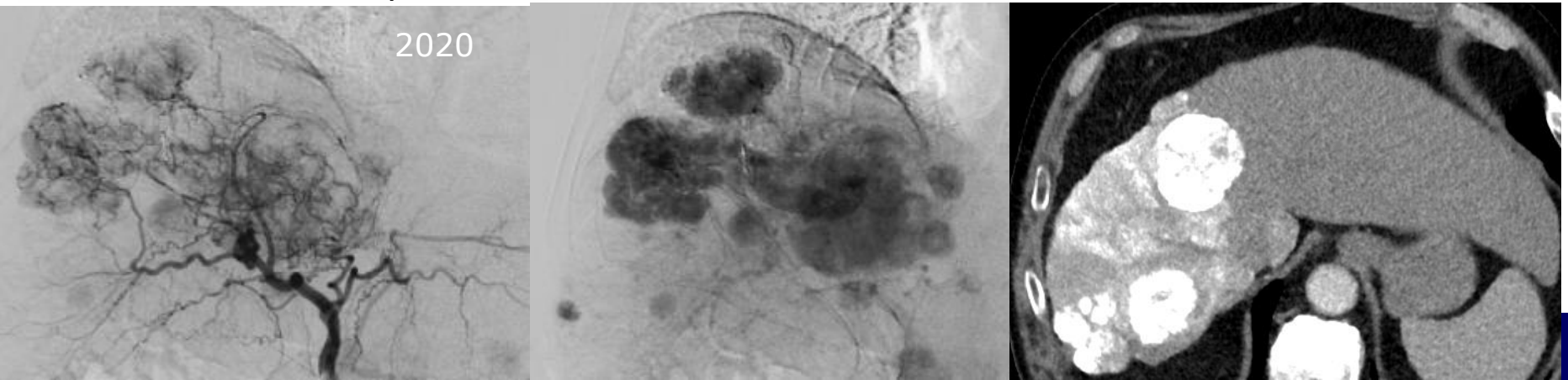
Multilocular HCC, superselective cTACE



70 yr. old pat.,
Child Pugh A, BSCL B
2015: DEB TACE

HCC ED 2015
OS >6 years

Multilocular HCC, unselective cTACE



II. TACE techniques: c-TACE

Embolisation

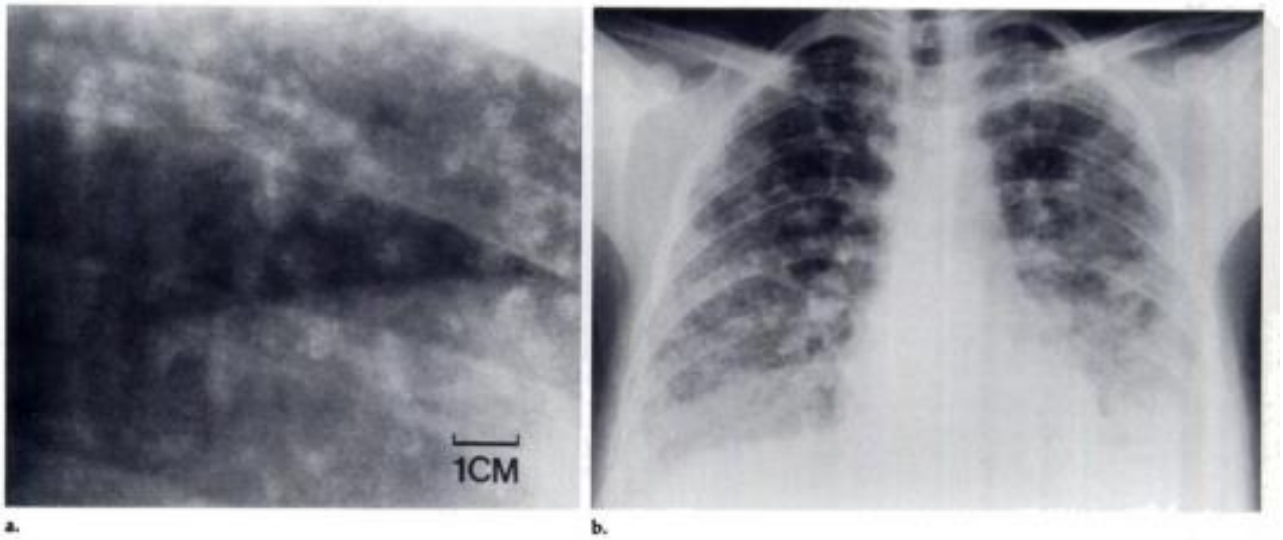
Jin Wook Chung, MD • Jae Hyung Park, MD • Jung-Gi Im, MD • Joon Koo Han, MD
Man Chung Han, MD

Radiology.
1993 Jun;187(3):689-93

Pulmonary Oil Embolism after Transcatheter Oily Chemoembolization of Hepatocellular Carcinoma[1]

"Pulmonary oil embolism develops in a large percentage of the patients in whom more than *20 mL of iodized oil* is used for TOCE of HCC".

"Large" droplets (70-100 µm) limit the risk of reaching the lung, which can cause subsequent toxicity, and increase tumour:non-tumoural liver uptake.



For safety reasons, it is recommended to use a total volume of less than 20mL in order to minimise the risk of pulmonary lipiodol embolism, which can be fatal.

II. TACE techniques: c-TACE

Embolisation

Kenichi Takayasu, MD • Yasuo Shima, MD • Yukio Muramatsu, MD • Noriyuki Moriyama, MD • Tatsuya Yamada, MD • Masatoshi Makuuchi, MD • Hiroshi Hasegawa, MD • Setsuo Hirohashi, MD

Radiology. 1987 May;163(2):345-51

Hepatocellular Carcinoma: Treatment with Intraarterial Iodized Oil with and without Chemotherapeutic Agents[1]

- 31 patients with HCC
- Lipiodol (group A, n = 6), lipiodol + doxorubicin hydrochloride (Adriamycin) (group B, n = 15), or chemoembolization+ lipiodol *followed by gelatin sponge (Gelfoam) particles* (group C, n = 10).
- group C demonstrated the *best therapeutic effects*, showing complete necrosis of the main lesion in 83% (P less than .01), daughter tumors in 53% (P less than .01), tumor thrombus in 17%, and foci of intracapsular invasion in 67%.

Table 3
Frequencies of Complete Necrosis of Main Tumor, Daughter Tumor, and Portal Vein Tumor Thrombus (Confirmed Microscopically)

Group	Complete Necrosis of Main Tumor			80% Necrosis of Invasive Tumors: Within Capsule	80% Necrosis of Invasive Tumors: Outside Capsule	Daughter Tumor			Portal Vein Tumor Thrombus
A (n = 6)	0/6 (0)	NS	P < .01	0/3 (0)	0/2 (0)	0/10 (0)	NS	P < .05	0/1 (0)
B (n = 15)	2/15 (13)			0/10 (0)	0/6 (0)	2/36 (6)			0/11 (0)
C (n = 10)*	10/12 (83)			2/3 (67)	0/1 (0)	10/19 (53)	P < .01		1/6 (17)

II. TACE techniques: c-TACE

Embolisation

- With regards to what degree of portal vein visualization should be achieved during lipiodol injection, it has been demonstrated that grade 2 segmental visualization correlate with lower recurrence rate.

Ultraselective Transcatheter Arterial Chemoembolization with a 2-F Tip Microcatheter for Small Hepatocellular Carcinomas: Relationship Between Local Tumor Recurrence and Visualization of the Portal Vein with Iodized Oil

Shiro Miyayama, MD, Osamu Matsui, MD, Masashi Yamashiro, MD, Yasuji Ryu, MD, Keiko Kaito, MD, Kumi Ozaki, MD, Taro Takeda, MD, Norihide Yoneda, MD, Kazuo Notsumata, MD, Daisyu Toya, MD, Nobuyoshi Tanaka, MD, and Takeshi Mitsui, MD

J Vasc Interv Radiol. 2007 Mar;18(3):365-76.

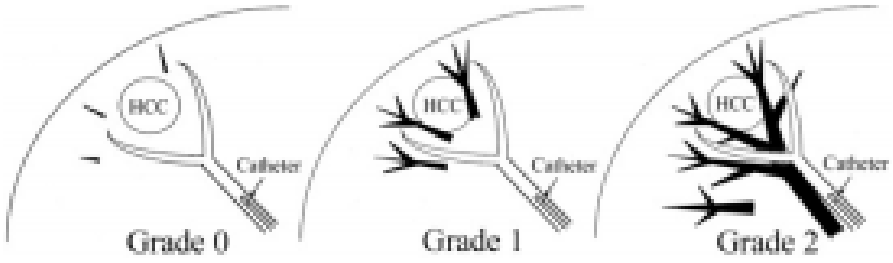
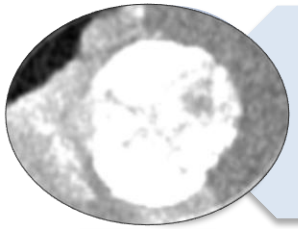


Figure 1. Schematic representation of the grades of portal vein visualization.

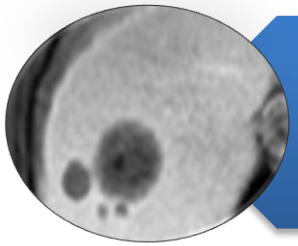
Grades of Portal Vein Visualization and Size of Tumors Treated with Ultraselective TACE

Tumor Group	No. of Tumors (n = 123)	Mean Tumor Diameter (cm)
Grade 2 (marked visualization)	53 (43.1)	2.2 ± 0.9*
Grade 1 (slight visualization)	52 (42.3)	1.8 ± 0.8
Grade 0 (no visualization)	18 (14.6)	1.3 ± 0.5

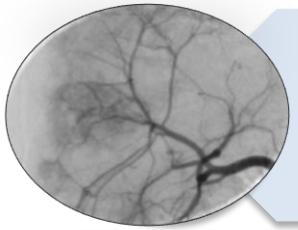
II. TACE techniques: DEM-TACE



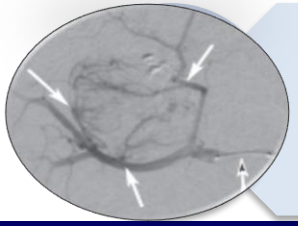
conventional TACE
(c-TACE)



drug-eluting microspheres (DEM-TACE)



Degradable Starch Microsphere (DSM-TACE)



balloon-occluded TACE (b-TACE)

II. TACE techniques DEM-TACE

- Drug-eluting microspheres are embolic agents that allow loading with *anthracyclines (doxorubicin, epirubicin, idarubicin)* and *irinotecan* through an ionic interaction of the cationic drug with the anionic functional groups of the microspheres.
- various types of drug-eluting microsphere (DEM) are commercially available for use with doxorubicin, with some differences in elution and suspension characteristics.
- maximum dose of *doxorubicin in a single session is 150 mg*. Drug dosage does not require adjustment according to body surface area (BSA) or weight. treatment priority should be given to the target lesion. *Cardiac toxicity of anthracyclines* is *cumulative* and observed above a certain threshold (i.e. *450mg/m² for doxorubicin).*

Cardiovasc Drugs Ther (2017) 31:63–75
DOI 10.1007/s10557-016-6711-0

REVIEW ARTICLE

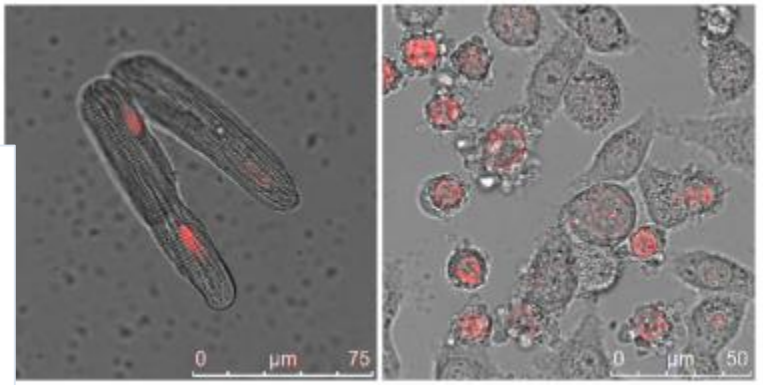
Anthracycline Chemotherapy and Cardiotoxicity

John V McGowan[1] · Robin Chung[1] · Angshuman Maulik[1] · Izabela Piotr
J Malcolm Walker[1] · Derek M Yellon[1]

Published online: 9 February 2017

Fig. 2 Doxorubicin staining shows sequestration in (L) cardiomyocytes and (R) malignant cervical cancer cells (courtesy Dr. I Piotrowska)

The basic mechanisms of cardiotoxicity may involve direct pathways for reactive oxygen species generation and topoisomerase 2 as well as other indirect pathways



II. TACE techniques DEM-TACE

Date: 07/30/2013
Author: Celine Chaix

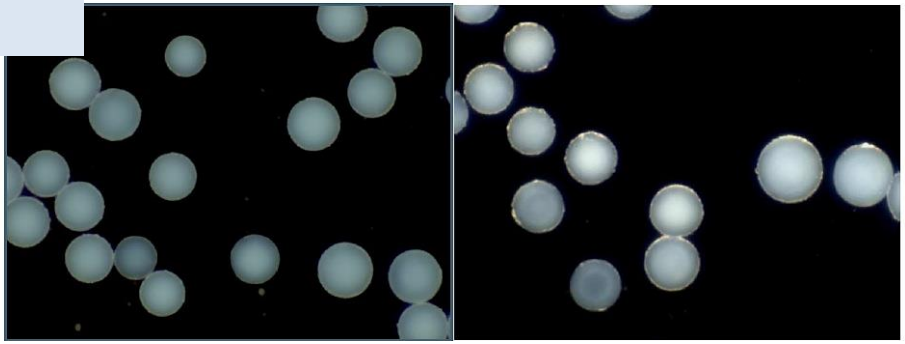
R&D -CC -1306 – HepaSphere -QuadraSphere & Campto : Stab i l ity study

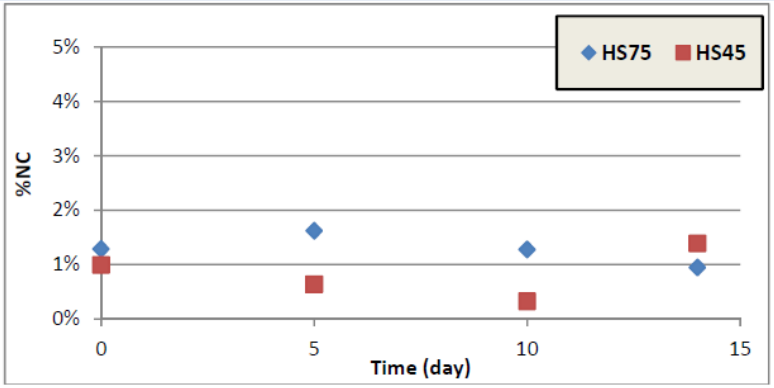
25mg HepaSphere-QuadraSphere 30-60µm +Irinotecan

At 2h, 5 days, 10 days and 14 days, a granulometry analysis was done on each vial of microspheres

The objective is to determine the stability and integrity of HepaSphere-QuadraSphere (HS-QS) when loaded with Irinotecan over a 14 days period of time.

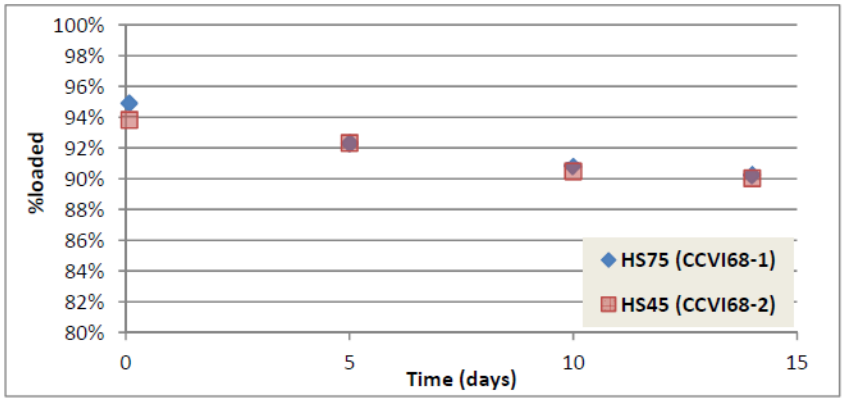
Picture 4 HS45 at day 10 (left) and 14 days (right)





As the percentages of non-compliant (NC) particles particles are not significantly increasing over the period of 14 days

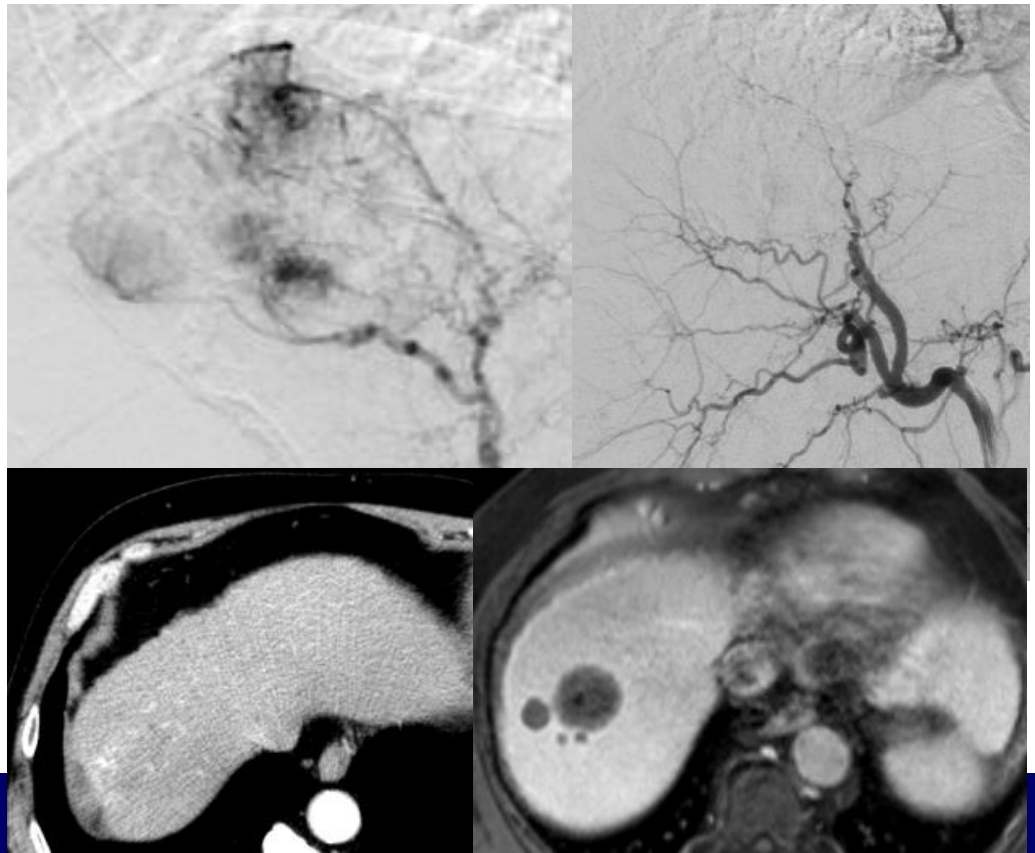
Graph 3 Loading



The concentration of irinotecan in the supernatant is slightly increasing over 14 days (the percentage loaded is so slightly decreasing) from 95 to 90% from 94 to 90% for HS45.

II. TACE techniques DEM-TACE

73 year old patient, multilocular HCC seg 7, DEB-TACE
50mg Doxorubicin, HepaSphere 30-60 microns



DEM are administered using a 1-3 ml syringe, mixed with contrast.

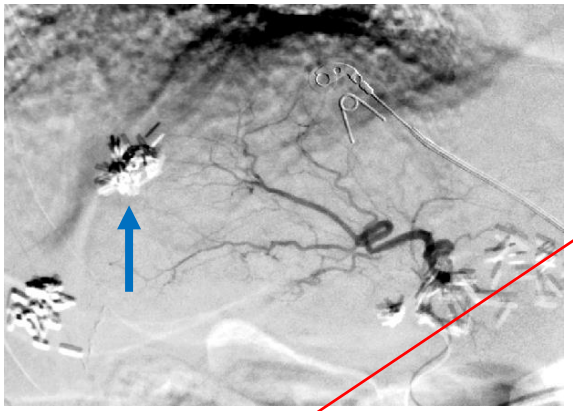
- slow infusion, smooth pulses
- avoid sedimentation by rotating the syringe or using a three-way stopcock
- if arterial stasis is not achieved: additional unloaded beads should be injected until the end point of arterial stasis has been reached.

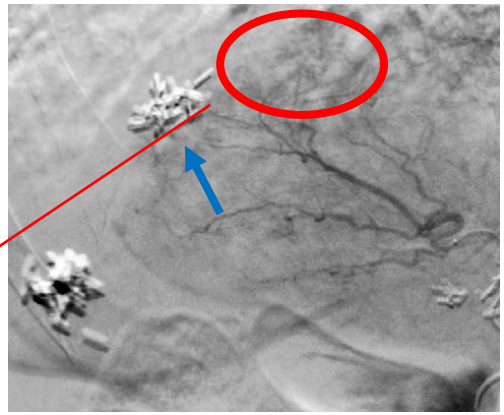
- >no definite evidence to support this statement and some groups recommend scheduling a repeat course of treatment.

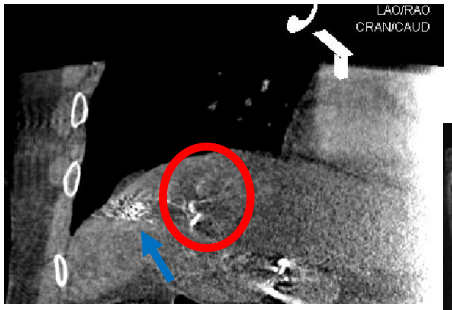
II. TACE techniques DEM-TACE

no technical differences in TACE of HCC, ICC and NETs.

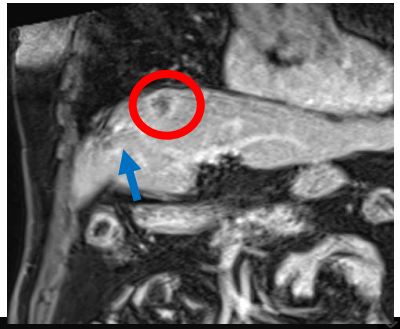
74 year old patient, multilocular HCC,
DEB-TACE seg 4a, 28mg Doxorubicin, HepaSphere 30-60 microns

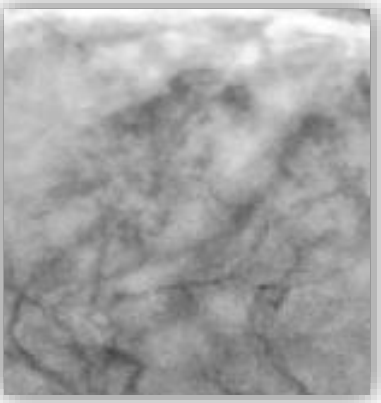


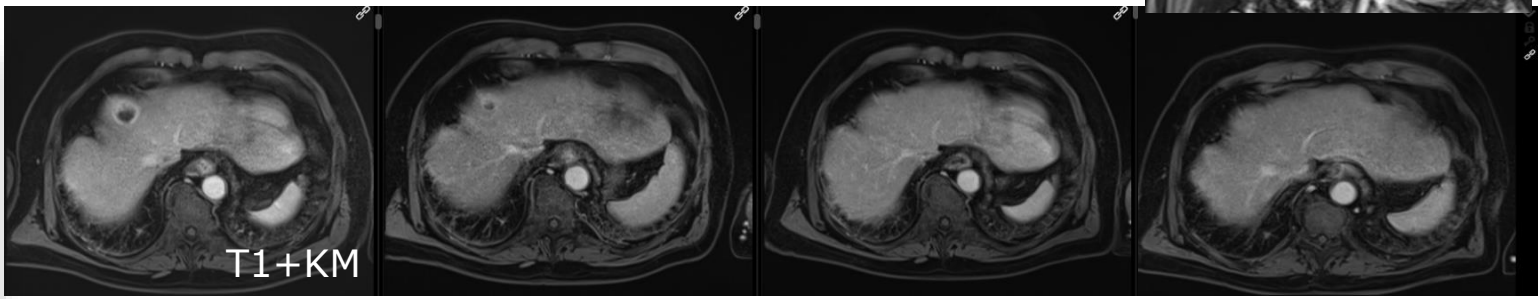




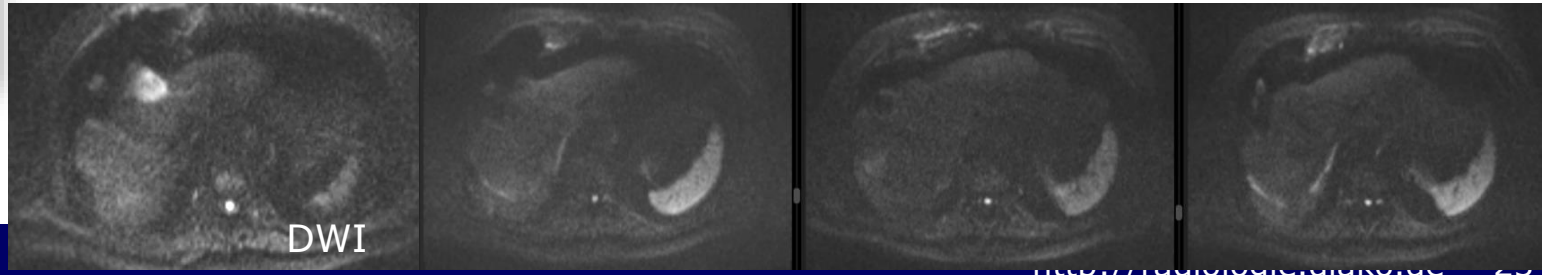
cone-beam CT







19.02.2019 02.04.2019 12.06.2020 16.09.2021



II. TACE techniques DEM-TACE

- since 2012: recommended size for a standard procedure usually 100-300 microns
- comparable safety and efficacy profile of particle sizes *smaller than 100 microns* (in *superselective catheterisation* of the feeder)
- unselective: increased risk of hepatobiliary complications.
- Combinations of different calibre beads can offer the advantage

Cardiovasc Intervent Radiol (2018) 41:587–593
https://doi.org/10.1007/s00270-017-1839-2

CIRSE CrossMark

CLINICAL INVESTIGATION INTERVENTIONAL ONCOLOGY

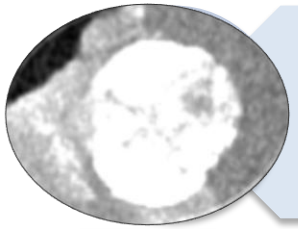
Safety and Feasibility of Chemoembolization with Doxorubicin-Loaded Small Calibrated Microspheres in Patients with Hepatocellular Carcinoma: Results of the MIRACLE I Prospective Multicenter Study

Götz Richter[1] · Boris Radeleff[2] · Christian Stroszczynski[3] · Philippe Pereira[4] · Thomas Helmberger[5] · Mark Barakat[6] · Peter Huppert[7]

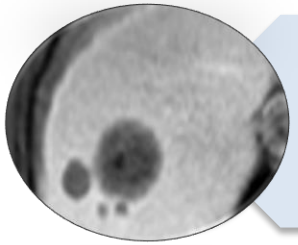
Received: 24 May 2017 / Accepted: 13 November 2017 / Published online: 22 November 2017

- DEB-TACE was performed with 75 µm Embozene TANDEM loaded with 150 mg of doxorubicin
- Tumor response or stable disease was achieved in 95% (20/21) of subjects.
- Freedom from tumor progression or death at 6 months was 76%.
- The one-year survival rate was 56% overall and 73% among patients without ascites at baseline.

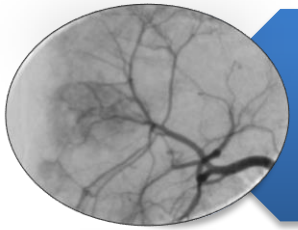
II. TACE techniques



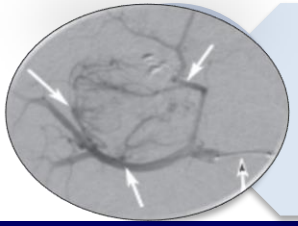
conventional TACE
(c-TACE)



drug-eluting microspheres (DEM-TACE, DEB-TACE)



Degradable Starch Microsphere (DSM-TACE)



balloon-occluded TACE (b-TACE)

III. TACE techniques
DSM-TACE

- Degradable starch microspheres (Embocept®, PharmaCept) consist of resorbable amilomer (hydrolysed potato starch) based particles, ranging around average 45 ±7 µm, that can be mixed with a wide range of chemotherapeutic agents
- The microspheres are enzymatically degraded by amylase in the blood with a half-life of about 35-50 minutes. The particles are completely resorbed after approximately 2 hours.
- The drug is usually mixed immediately before administration using 4mL out of a 7.5 ml DSM vial, then mixed in suspension with adjunctive contrast media (around 15-20 ml).
- The treatment consists of administering the total predicted dose of drug, followed by the residual part of the DSM vial, used as unloaded temporary embolic agent.
- Embolisation to stasis is a crucial end-point to allow adequate drug absorption within the target lesion.

La radiologia medica
https://doi.org/10.1007/s11547-019-01076-y

ABDOMINAL RADIOLOGY

Sequential dual-phase cone-beam CT is able to intra-procedurally predict the one-month treatment outcome of multi-focal HCC, in course of degradable starch microsphere TACE

Pierleone Lucatelli[1] · Gianluca De Rubeis[1] · Fabrizio Basilico[1] · Luca Ginanni Corradini[1] · Mario Corona[1] · Mario Bezzi[1] · Carlo Catalano[1]

Received: 23 January 2019 / Accepted: 23 August 2019

- multiple times, at least twice for each treatment site.
- the lobe with greater tumour involvement is treated first, followed after 14 days by the contralateral lobe.
- After two more weeks the treatment cycle can be repeated

III. TACE techniques
DSM-TACE

European Radiology
https://doi.org/10.1007/s00330-018-5692-8

INTERVENTIONAL

TACE with degradable starch microspheres (DSM-TACE) as second-line treatment in HCC patients dismissing or ineligible for sorafenib

Roberto Iezzi[1] · Maurizio Pompili[2] · Emanuele Rinninella[2] · Eleonora Annicchiarico[2] · Matteo Garcovich[2] · Lucia Cerrito[2] · Francesca Ponziani[2] · AnnaMaria De Gaetano[1] · Massimo Siciliano[2] · Michele Basso[3] · Maria Assunta Zocco[2] · GianLodovico Rapaccini[2] · Alessandro Posa[1] · Francesca Carchesio[1] · Marco Biolato[2] · Felice Giuliante[4] · Antonio Gasbarrini[2] · Riccardo Manfredi[1] · the HepatoCatt Study Group

Received: 11 June 2018 / Revised: 17 July 2018 / Accepted: 31 July 2018

- 40 BCLC stage B or C patients (with intermediate or locally advanced HCC dismissing or ineligible for sorafenib administration
- No intra/peri-procedural death/major complications occurred. No signs of liver failure or systemic toxicity were detected.
- 1-year follow-up, ODC of 52.5%, PFS was 6.4 months, median OS of 11.3 months.

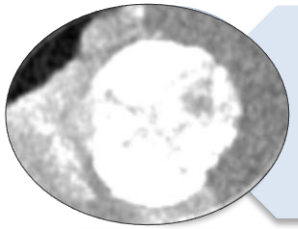
Table 2 Overall survival: subgroup evaluation

Subgroup	1-year survival rate (%)	2-year survival rate (%)	Median OS (months)
BCLC-B	64.2	30.4	11.7
BCLC-C	55.3	37.3	9.3
CHILD-A	69.4	31.7	12.3
CHILD-B	57.1	39.2	9.1
BCLC-B/CHILD-A	69.4	60.7	12.9 *
BCLC-B/CHILD-B	69.4	50.6	10.8
BCLC-C/CHILD-A	66.7	38.9	9.4
BCLC-C/CHILD-B	37.5	31.2	6.5

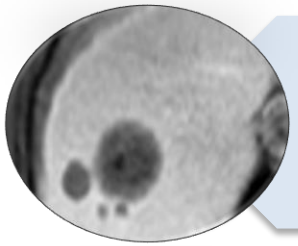
* Significantly higher ($p = 0.02$) than that obtained in the BCLC-C/CHILD-B subgroup

The main advantage of DSM TACE is that it may be used in patients with a bilirubin >3 mg/dL and portal vein thrombosis

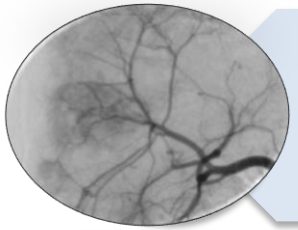
II. TACE techniques
B-TACE



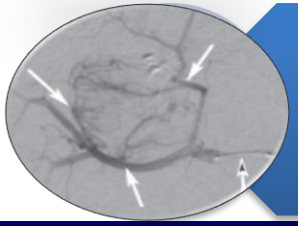
conventional TACE
(c-TACE)



drug-eluting microspheres (DEM-TACE, DEB-TACE)



Degradable Starch Microsphere (DSM-TACE)

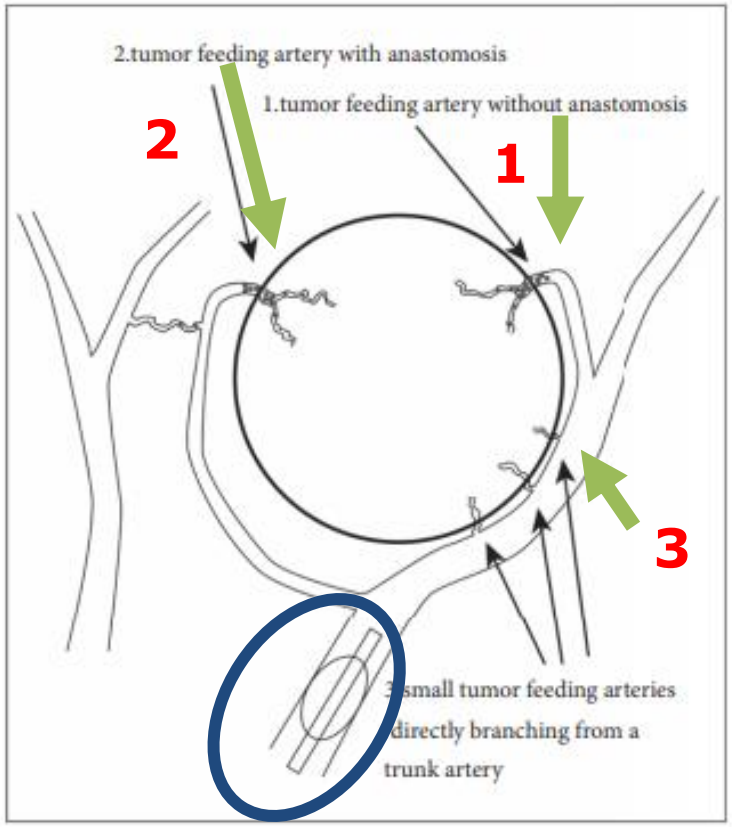


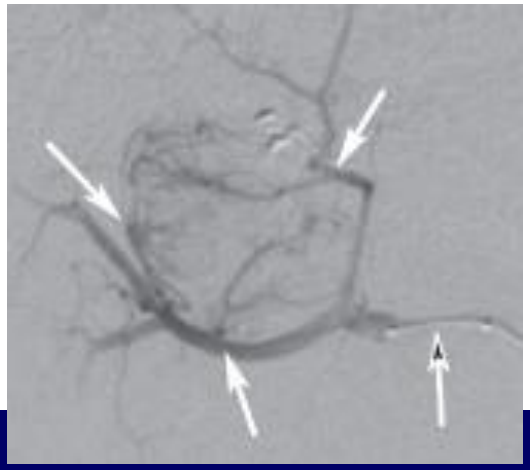
balloon-occluded TACE (b-TACE)

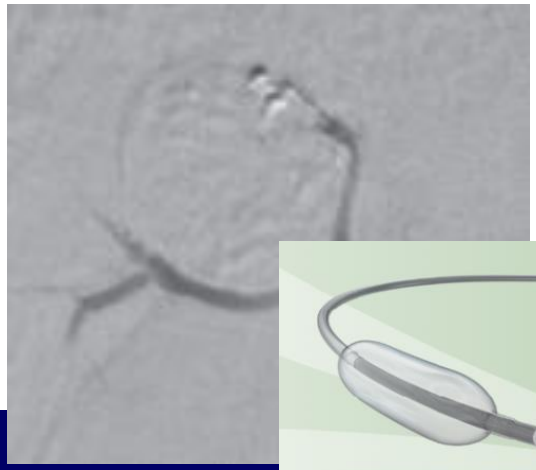
II. TACE techniques
B-TACE

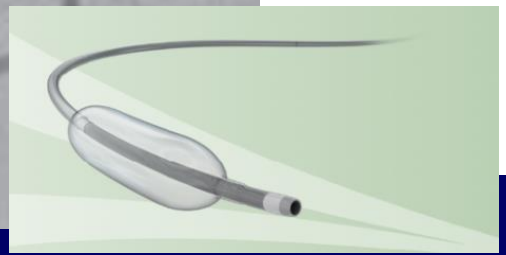
Irie T, Takahashi N, Kamoshida T. Balloon-Occluded Trans-Arterial Chemoembolization Technique with Alternate Infusion of Cisplatin and Gelatin Slurry for Small Hepatocellular Carcinoma Nodules Adjacent to the Glisson Sheath. Biomed Res Int. 2019 May 9;2019:8350926.

- 2013, Irie et al.
- temporary occlusion
- performing a pressure driven embolization
- Micro-balloons (Occlusafe, Terumo, Japan) are positioned proximal to all lesion feeders in order to maximise efficacy.
- invasive arterial pressure is monitored to detect a pressure drop. Mean arterial pressure threshold below which the b-TACE effect will perform optimally, is 62 mmHg
- micro-balloon maximum diameter is 4 mm.









RAIB-TACE (repeated alternate infusion of cisplatin solution and gelatin slurry distal to balloon occlusion)

II. TACE techniques
Radiopaque beads

- DC Bead LUMI™ (Biocompatibles UK Ltd, UK) is a drug-eluting technology with iodine incorporated into its chemical structure, ensuring that it is permanently radiopaque
- Few studies have been published with radiopaque beads in humans. They showed safety and response rates comparable to non-radiopaque beads, although no randomized or comparative data are available.
- difficulty to ensure reliable imaging follow-up using CT
- very different pharmacokinetic profile of drug elution compared to non-radiopaque beads

- all prior phase I/II data published on doxorubicin-eluting microspheres are not valid with radiopaque beads, which theoretically necessitates specific clinical investigations.

Cardiovasc Intervent Radiol (2019) 42:1563–1570
https://doi.org/10.1007/s00270-019-02317-3

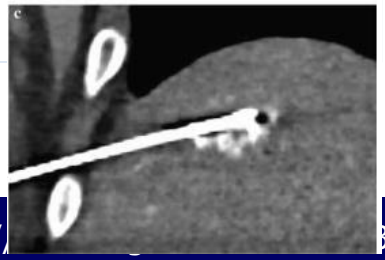
CIRSE

CLINICAL INVESTIGATION INTERVENTIONAL ONCOLOGY

Early Experience of Trans-arterial Chemo-Embolisation for Hepatocellular Carcinoma with a Novel Radiopaque Bead

John Reicher[1] · Sebastian Mafeld[1] · Georgia Priona[1] · Helen L. Reeves[1] · Derek M. Manas[1] · Ralph Jackson[1] · Peter Littler[1]

- Objective response rates (mRECIST) at 1, 3 and 6 months were 32/35 (91.4%), 21/24 (87.5%) and 12/15 (80%).
- Complete response rates at 1, 3 and 6 months were 16/35 (45.7%), 12/24 (50%) and 9/15 (60%).
- The embolised territory was visible on intra-operative and follow-up CT imaging in all patients.
- The radiopaque beads were used as a fiducial marker to guide ablation in 5/40 patients (12.5%).



III. Outcomes
Hepatocellular Carcinoma (HCC)

Intermediate-stage HCC and grade of response to cTACE in each subgroup

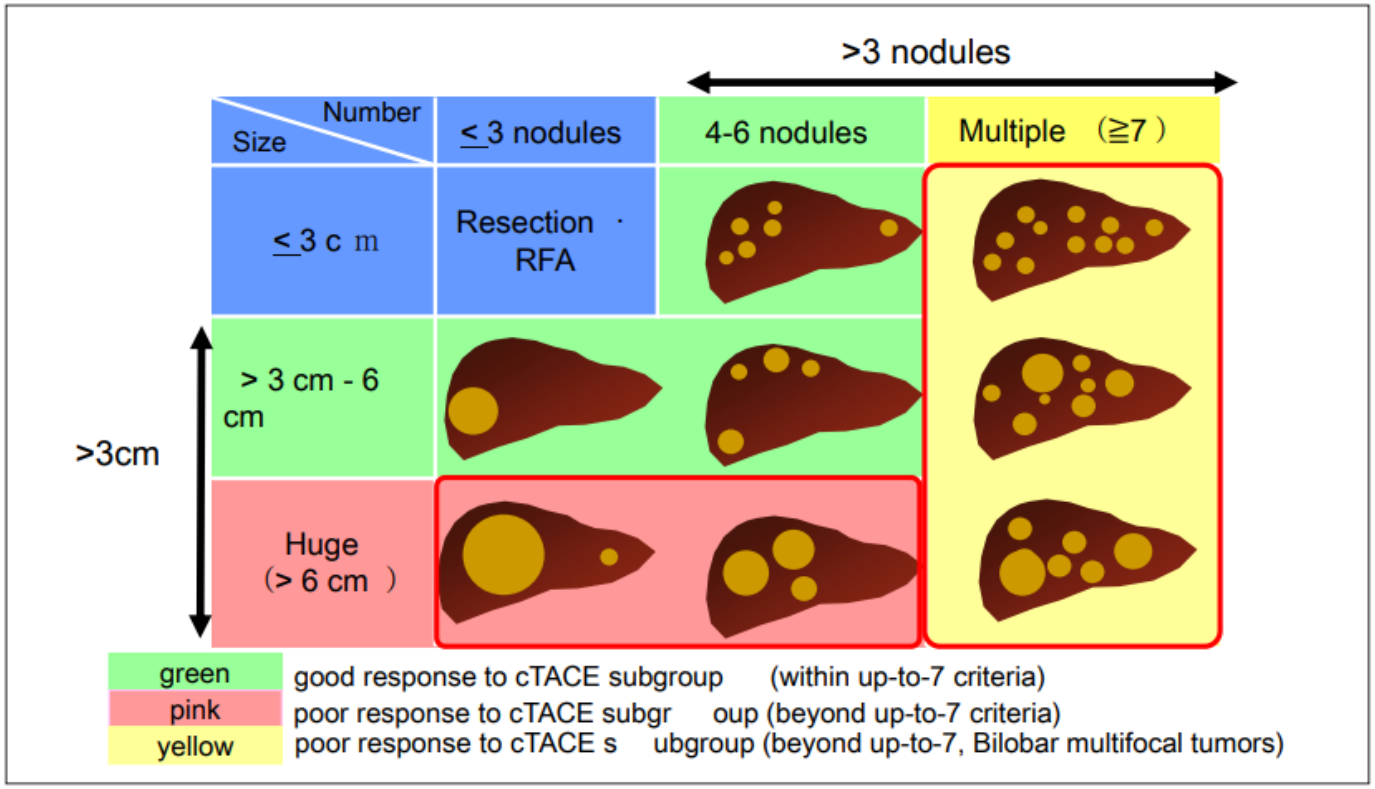


Fig. 2. Heterogeneity of intermediate-stage HCC and grade of response to TACE in each subgroup. cTACE, conventional transarterial chemoembolization.

Kudo, M.; Han, K.H. et al. A changing paradigm for the treatment of intermediate-stage hepatocellular carcinoma: Asia-Pacific Primary Liver Cancer Expert Consensus Statements. Liver Cancer 2020, 9, 245–260.

- size, numbers of lesions (single vs multifocal; uni-lobar vs bilobar)
- percentage volume of tumour spread
- HCC lesions greater than 3 cm: need for multiple treatments,
- tumour involvement >50% of the liver volume: poor prognosis
- Presence and extension of portal vein thrombosis, influences prognosis and risk of the procedure

III. Outcomes
Hepatocellular Carcinoma (HCC)

cTACE

Randomized Controlled Trial of Transarterial Lipiodol Chemoembolization for Unresectable Hepatocellular Carcinoma

Chung-Mau Lo, Henry Ngan, Wai-Kuen Tso, Chi-Leung Liu, Chi-Ming Lam, Ronnie Tung-Ping Poon, Sheung-Tat Fan, and John Wong

HEPATOLOGY, Vol. 35, No. 5, 2002

- Chemoembolization resulted in a marked tumor response, and the actuarial survival was significantly better in the *chemoembolization group (1 year, 57%; 2 years, 31%; 3 years, 26%)* than in the control group (1 year, 32%; 2 years, 11%; 3 years, 3%; P =.002).

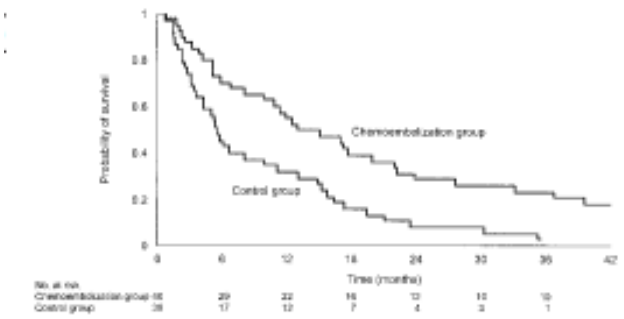


Fig. 2. Probability of survival in patients treated with chemoembolization and in patients of the control group (log-rank test, $P = .002$).

ARTICLES

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

*Josep M Llovet, Maria Isabel Real, Xavier Montaña, Ramon Planas, Susana Coll, John Aponte, Carmen Ayuso, Margarita Sala, Jordi Muchart, Ricard Solà, Joan Rodés, Jordi Bruix, for the Barcelona Clínic Liver Cancer Group**

THE LANCET • Vol 359 • May 18, 2002 • www.thelancet.com

- chemoembolisation had survival benefits compared with conservative treatment (hazard ratio of death 0.47 [95% CI 0.25-0.91], p=0.025).
- Survival probabilities at 1 year and 2 years were 75% and 50% for embolisation; *82% and 63% for chemoembolisation*, and 63% and 27% for control (chemoembolisation vs control p=0.009).
- 112 patients; early interrupted for cTACE superiority over control group

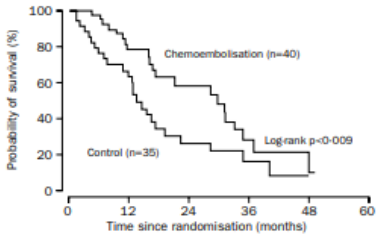


Figure 3: **Survival curves of the chemoembolisation and control groups**

http:/

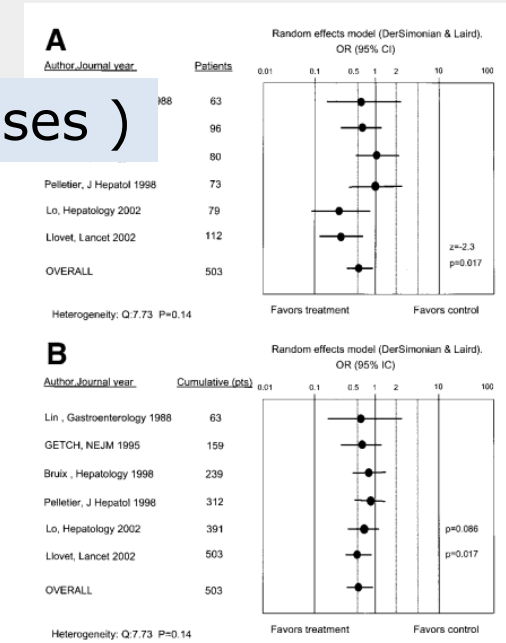
III. Outcomes
Hepatocellular Carcinoma (HCC)

cTACE (meta-analyses)

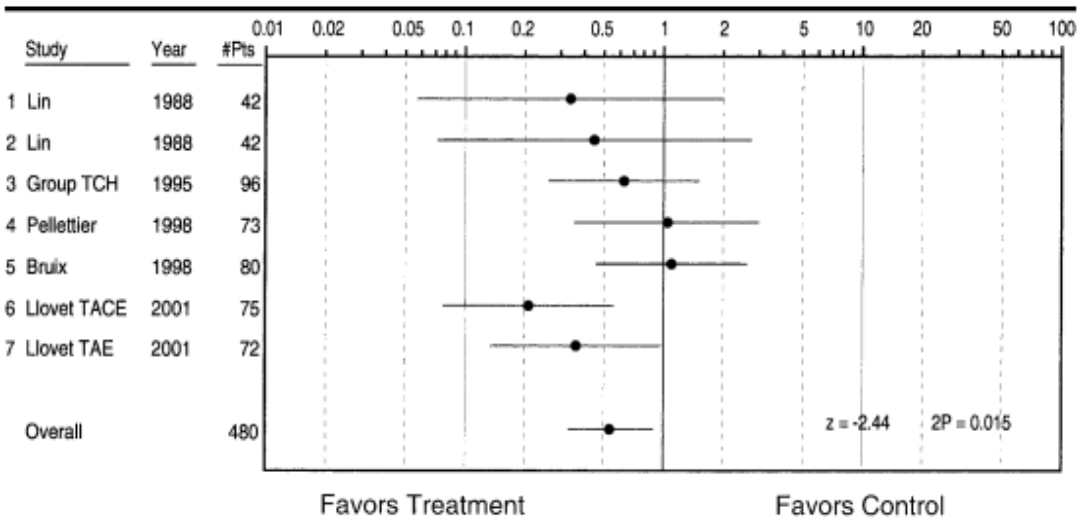
Systematic Review of Randomized Trials f
Unresectable Hepatocellular Carcinoma:
Chemoembolization Improves Survival

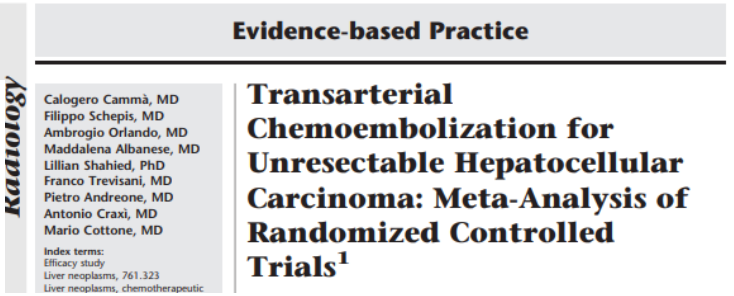
Josep M. Llovet and Jordi Bruix for the Barcelona-Clínic Liver Cancer Group

HEPATOLOGY, Vol. 37, No. 2, 2003



- Arterial embolization improved 2-year survival compared with control (odds ratio [OR], 0.53; 95% confidence interval [CI], 0.32-0.89; P =.017). Sensitivity analysis showed a *significant benefit of chemoembolization with cisplatin or doxorubicin* (OR, 0.42; 95% CI, 0.20-0.88) but none with embolization alone (OR, 0.59; 95% CI, 0.29-1.20).





Radiology. 2002 Jul;224(1):47-54.

- Chemoembolization significantly *reduced the overall 2-year mortality rate* (odds ratio, 0.54; 95% CI: 0.33, 0.89; P =.015) compared with nonactive treatment.

III. Outcomes Hepatocellular Carcinoma (HCC)

DEM-TACE vs cTACE

Cardiovasc Intervent Radiol (2010) 33:41–52
DOI 10.1007/s00270-009-9711-7

CLINICAL INVESTIGATION

Prospective Randomized Study of Doxorubicin-Eluting-Bead Embolization in the Treatment of Hepatocellular Carcinoma: Results of the PRECISION V Study

Johannes Lammer · Katarina Malagari · Thomas Vogl · Frank Pilleul · Alban Denys · Anthony Watkinson · Michael Pitton · Geraldine Sergent · Thomas Pfammatter · Sylvain Terraz · Yves Benhamou · Yves Avajon · Thomas Gruenberger · Maria Pomoni · Herbert Langenberger · Marcus Schuchmann · Jerome Dumortier · Christian Mueller · Patrick Chevallier · Riccardo Lencioni · On Behalf of the PRECISION V Investigators

- The DEB group showed higher rates of complete response, objective response, and disease control compared with the cTACE group (27% vs. 22%, 52% vs. 44%, and 63% vs. 52%, respectively). *The hypothesis of superiority was not met (one-sided P = 0.11).*

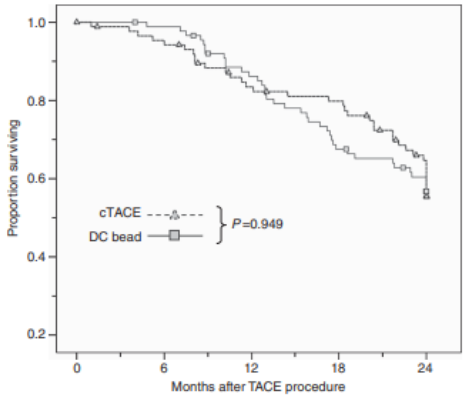
- DEB TACE *improved tolerability, with a significant reduction in serious liver toxicity* (P < 0.001) and a *significantly lower rate of doxorubicin-related side effects* (P = 0.0001).

Randomised controlled trial of doxorubicin-eluting beads *vs* conventional chemoembolisation for hepatocellular carcinoma

British journal of cancer, 2014 111(2):255-264

R Golfieri[1], E Giampalma[1], M Renzulli[*,1], R Cioni[2], I Bargellini[2], C Bartolozzi[2], A D Breatta[3], G Gandini[3], R Nani[4], D Gasparini[5], A Cucchetti[6], L Bolondi[6] and F Trevisani[6] on behalf of the PRECISION ITALIA STUDY GROUP[7]

- 89 underwent DEB-TACE and 88 cTACE
- No differences were found in local and overall tumour response
- The median TTP (*time-to-tumour progression) was 9 months in both arms.*
- The 1- and 2-year survival rates were 86.2% and 56.8% after DEB-TACE and 83.5% and 55.4% after cTACE (*P=0.949*).



At risk	0	3	6	9	12	18	24
cTACE	88	85	82	74	69	65	42
DC bead	89	88	87	79	74	58	47

Figure 4. Patient survival after cTACE (triangle plot) and DEB-TACE (square plot).

III. Outcomes Hepatocellular Carcinoma (HCC)

DEM-TACE vs cTACE

Digestive and Liver Disease xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld

Review Article

Drug-eluting beads versus conventional chemoembolization for the treatment of unresectable hepatocellular carcinoma: A meta-analysis

Antonio Facciorusso*, Marianna Di Maso, Nicola Muscatiello

Dig Liver Dis. 2016 Jun;48(6):571-7

- Non-significant trends in favor of drug-eluting beads chemoembolization were observed as for 1-year (odds ratio: 0.76, 0.48-1.21, p=0.25), 2-year (odds ratio: 0.68, 0.42-1.12, p=0.13) and 3-year survival (odds ratio: 0.57, 0.32-1.01, p=0.06).

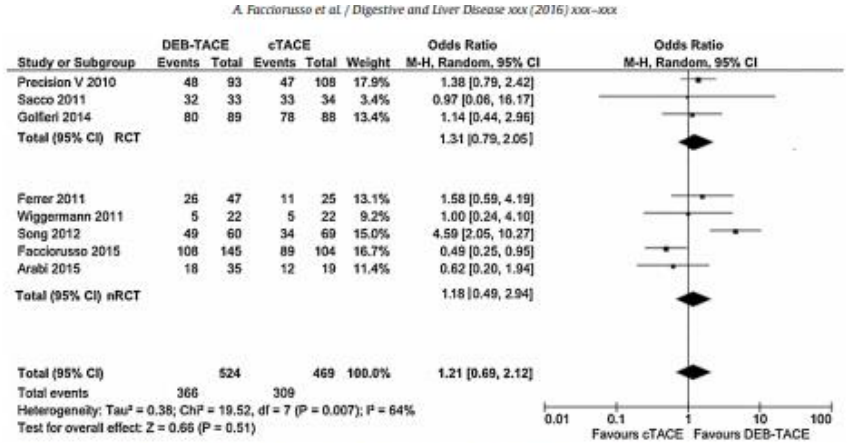


Fig. 3. Forest plot comparing objective response rate for DEB-TACE to that for cTACE. Random effect DerSimonian Laird model showed a summary odds ratio slightly higher after DEB-TACE without reaching the statistical significance. High heterogeneity was found. DEB-TACE, drug-eluting bead transarterial chemoembolization; cTACE,

III. Outcomes Hepatocellular Carcinoma (HCC)

DEM-TACE vs cTACE

RESEARCH ARTICLE PLoS One. 2020 Feb 19;15(2):e0227475.

Transarterial strategies for the treatment of unresectable hepatocellular carcinoma: A systematic review

Biao Yang[1,2☯]*, Jie Liang[3☯], ZiYu Qu[2], FangYun Yang[2], ZhengYin Liao[2]*, HongFeng Gou[2]*

- DEB-TACE has a better OS at 1 year than cTACE (RR 0.79, 95% CI 0.67-0.93, p = 0.006), 2 years (RR 0.89; 95% CI 0.81-0.99, p = 0.046), and 3 years (RR 0.89; 95% CI 0.81-0.99, p = 0.035).
- TARE has a better OS than cTACE at 2 years (RR 0.87; 95% CI 0.80-0.95, p = 0.003) and 3 years (RR 0.90; 95% CI 0.85-0.96, p = 0.001).
- DEB-TACE has a better OS than TARE at 2 years (RR 0.40; 95% CI 0.19-0.84, p = 0.016).

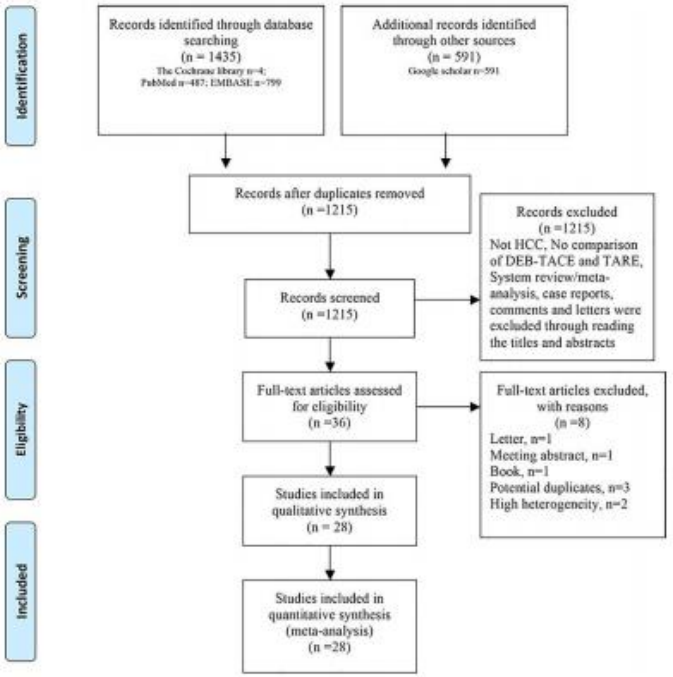
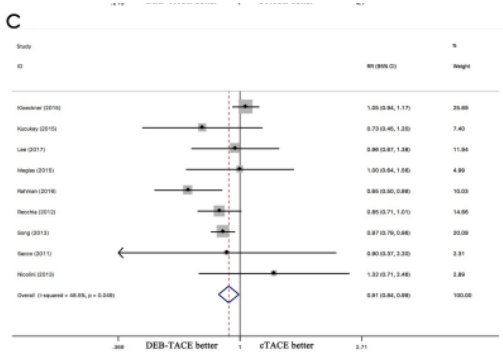


Fig 1. Flow chart depicting the study selection process.



The current meta-analysis suggests that DEB-TACE is superior to both TARE and cTACE in terms of OS. TARE has significantly lower complications than both DEB-TACE and cTACE for patients with HCC.

III. Outcomes Hepatocellular Carcinoma (HCC)

DSM-TACE

www.impactjournals.com/oncotarget/ Oncotarget, 2017, Vol. 8, (No. 42), pp: 72613-72620

Research Paper

Transarterial chemoembolization (TACE) with degradable starch microspheres (DSM) in hepatocellular carcinoma (HCC): multi-center results on safety and efficacy

Andreas Schicho[1], Philippe L. Pereira[2], Michael Haimerl[1], Christoph Niessen[1], Katharina Michalik[1], Lukas P. Beyer[1], Christian Stroszczynski[1] and Philipp Wiggermann[1]

- A national, multi-center observational study on the safety and efficacy of DSM-TACE for the treatment of intermediate HCC
- 179 DSM-TACE procedures in 50 patients were included
- Thus, the objective response rate was 44% (n=22) and disease control rate was 70% (n=35).

INTERVENTIONAL

TACE with degradable starch microspheres (DSM-TACE) as second-line treatment in HCC patients dismissing or ineligible for sorafenib

Roberto Iezzi[1] · Maurizio Pompili[2] · Emanuele Rinninella[2] · Eleonora Annicchiarico[2] · Matteo Garcovich[2] · Lucia Cerrito[2] · Francesca Ponziani[2] · AnnaMaria De Gaetano[1] · Massimo Siciliano[2] · Michele Basso[3] · Maria Assunta Zocco[2] · GianLodovico Rapaccini[2] · Alessandro Posa[1] · Francesca Carchesio[1] · Marco Biolato[2] · Felice Giuliante[4] · Antonio Gasbarrini[2] · Riccardo Manfredi[1] · the HepatoCatt Study Group

Eur Radiol. 2019 Mar;29(3):1285-1292

- 1-year follow-up: ODC (overall disease control) of 52.5%
- PFS was 6.4 months with a median OS of 11.3 months.

Table 2 Overall survival: subgroup evaluation

Subgroup	1-year survival rate (%)	2-year survival rate (%)	Median OS (months)
BCLC-B	64.2	30.4	11.7
BCLC-C	55.3	37.3	9.3
CHILD-A	69.4	31.7	12.3
CHILD-B	57.1	39.2	9.1
BCLC-C/CHILD-A	66.7	38.9	9.4
BCLC-C/CHILD-B	37.5	31.2	6.5

DSM-TACE was employed for HCC as first line

or second line treatment (after Sorafenib cessation)

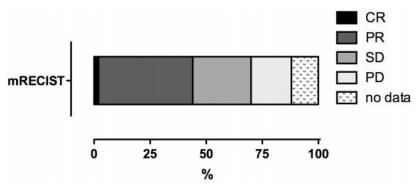


Figure 2: Tumor response of HCC to DSM-TACE. CR = complete response, PR = partial response, SD = stable disease, PD = progressive disease.

III. Outcomes Hepatocellular Carcinoma (HCC)

DSM-TACE

Original Article

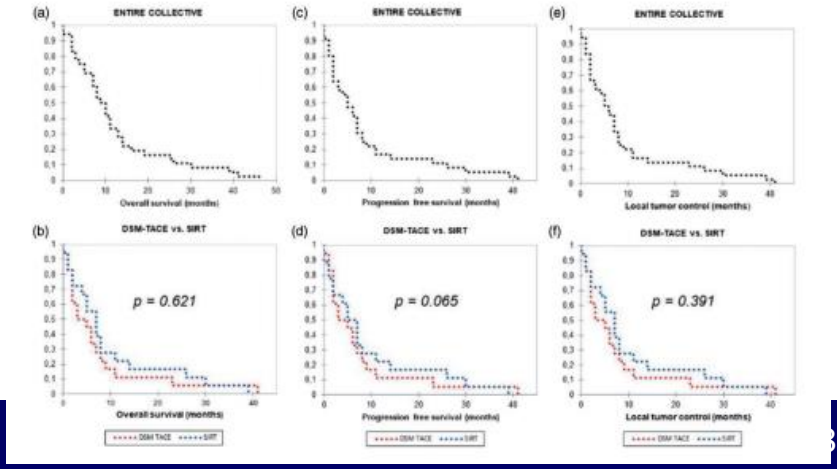
Trans-arterial chemoembolization with degradable starch microspheres (DSM-TACE) versus selective internal radiation therapy (SIRT) in multifocal hepatocellular carcinoma

Timo A Auer, Martin Jonczyk, Federico Collettini, Adrian Marth, Gero Wieners, Bernd Hamm and Bernhard Gebauer

Acta Radiol. 2021 Mar;62(3):313-321.

- 36 patients without portal vein invasion, treated between May 2014 and May 2018, were enrolled retrospectively
- PFS was 6 months for the SIRT and 4 months for the DSM-TACE cohort (P = 0.065). Although not significantly, LTC was lower (4 months) in the SIRT compared to the DSM-TACE cohort (7 months; P = 0.391).
- When DSM-TACE was performed ≥3 times (n = 11), OS increased, however without statistical difference compared to SIRT, to 11 months, PFS to 7 months, and LTC to 7 months.

DSM-TACE might be an alternative to SIRT in multifocal HCC patients as OS, progression-free *survival (PFS) and local tumor control (LTC) did not differ significantly and toxicity profiles seem to be comparable*



III. Outcomes Hepatocellular Carcinoma (HCC)

b-TACE

Cardiovasc Intervent Radiol. 2016 Mar;39(3):359-66.

Hepatology Research 2016; **46**: E60–E69 doi: 10.1111/hepr.12527

Original Article

Efficacy of a microballoon catheter in transarterial chemoembolization of hepatocellular carcinoma using miriplatin, a lipophilic anticancer drug: Short-term results

Masahiro Ogawa,[1] Kentaro Takayasu,[1] Midori Hirayama,[1] Takao Miura,[1] Katsuhiko Shiozawa,[1] Masahisa Abe,[1] Naoki Matsumoto,[1] Hiroshi Nakagawara,[1] Shu Ohshiro,[1] Toshiki Yamamoto,[1] Naohide Tanaka,[1] Mitsuhiko Moriyama,[1] Haruomi Mutou,[2] Yoshinobu Yamamoto[3] and Toshiyuki Irie[4]

- B-TACE was performed for 62 HCC nodules in 33 patients
- The therapeutic efficacy after 4-12 weeks was evaluated in 59 nodules in the B-TACE group and in 37 nodules in the C-TACE group. Of these nodules, TE4 occurred in 29 (49.2%) in the B-TACE group and in 10 (27%) in the C-TACE group.
- *Local efficacy was significantly higher in nodules treated by B-TACE than by C-TACE.* The side-effects on hepatic function were similar in the two groups.

Cardiovasc Intervent Radiol
DOI 10.1007/s00270-015-1237-6

CLINICAL INVESTIGATION

Initial Experience with Balloon-Occluded Trans-catheter Arterial Chemoembolization (B-TACE) for Hepatocellular Carcinoma

Mitsunari Maruyama[1] · Takeshi Yoshizako[1] · Tomonori Nakamura[1] · Megumi Nakamura[1] · Rika Yoshida[1] · Hajime Kitagaki[1]

- B-TACE group (50 cases) was compared with C-TACE group (50 cases).
- *B-TACE caused severe adverse events* (liver abscess and infarction) in patients with bile duct dilatation.

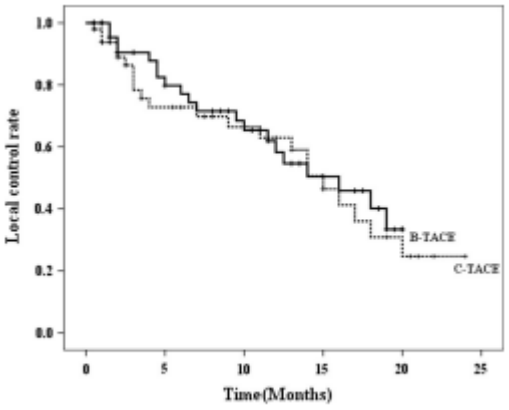


Fig. 1 Local control rate between B-TACE and C-TACE

III. Outcomes Hepatocellular Carcinoma (HCC)

DEM TACE + b-TACE

Cardiovasc Intervent Radiol (2019) 42:853–862
https://doi.org/10.1007/s00270-019-02192-y

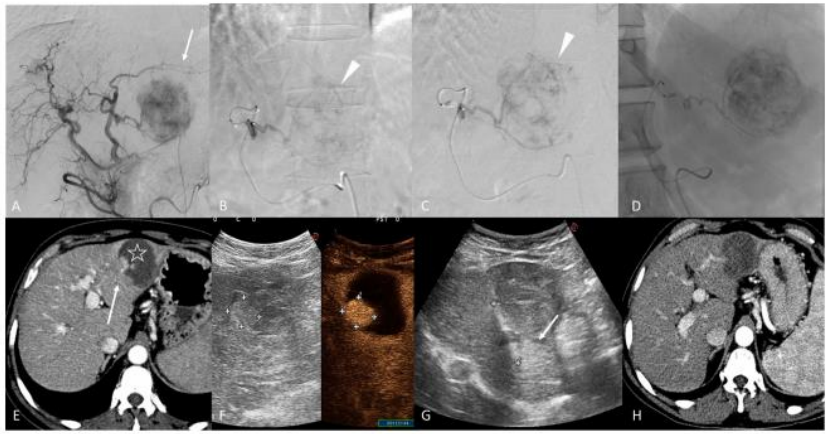
CLINICAL INVESTIGATION INTERVENTIONAL ONCOLOGY

Balloon-Occluded Transcatheter Arterial Chemoembolization (b-TACE) for Hepatocellular Carcinoma Performed with Polyethylene-Glycol Epirubicin-Loaded Drug-Eluting Embolics: Safety and Preliminary Results

Pierleone Lucatelli[1] · Luca Ginnani Corradini[1] · Gianluca De Rubeis[1] · Bianca Rocco[1] · Fabrizio Basilico[1] · Alessandro Cannavale[1] · Pier Giorgio Nardis[1] · Mario Corona[1] · Luca Saba[2] · Carlo Catalano[1] · Mario Bezzi[1]

Goldman DT, Singh M, Patel RS, et al. Balloon-Occluded Transarterial Chemoembolization for the Treatment of Hepatocellular Carcinoma: A Single-Center US Preliminary Experience. (*J Vasc Interv Radiol* 2019; 30:342–346)

- This is a single-centre, single-arm, retrospective study with 6-month follow-up. 22 patients (Child–Pugh A 68%, B 32%)
- Complete response at 1 and 3-6 months was 44.8% (13/29) and 52.9% (9/17), respectively.
- Partial response at 1 and 3-6 months was 55% (16/29) and 4/17 (23.5%), respectively. Among partial responder patients, the average percentage of tumour volume reduction was 64.9 ± 27.3%.



Epirubicin-loaded PEG microsphere b-TACE is technically feasible, safe and effective procedure for HCC treatment.

III. Outcomes Hepatocellular Carcinoma (HCC)

b-TACE

Cardiovasc Intervent Radiol (2021) 44:1048–1059
https://doi.org/10.1007/s00270-021-02805-5

CIRSE

CLINICAL INVESTIGATION — INTERVENTIONAL ONCOLOGY

Retrospective European Multicentric Evaluation of Selective Transarterial Chemoembolisation with and without Balloon-Occlusion in Patients with Hepatocellular Carcinoma: A Propensity Score Matched Analysis

Rita Golfieri[1,2] · Mario Bezzi[3] · Gontran Verset[4] · Fabio Fucilli[5] · Cristina Mosconi[1] · Alberta Cappelli[1] · Alexandro Paccapelo[1] · Pierleone Lucatelli[3] · Nicolas Magand[6] · Agnes Rode[6] · Thierry De Baere[7]

Table 3 Number of retreatments in the total patient population before and after propensity score matching (PSM) for number of nodules, age, gender, type of TACE and Child–Pugh class

Before PSM	Total no. of patients (n = 525)		Non-B-TACE (n = 434)		B-TACE (n = 91)		P
Retreatment	122	(23.2%)	113	(26.0%)	9	(9.9%)	0.001[A]
After PSM	Total no. of patients (n = 182)		Non-B-TACE (n = 91)		B-TACE (n = 91)		P
Retreatment	29	(15.9%)	20	(22.0%)	9	(9.9%)	0.041[A]

[A]Fisher's Exact test

- retrospective European multicentric registry
- 96 patients b-TACE vs 434 patients non b-TACE (cTACE or DEM-TACE).
- better complete response at 1 month (59.3% vs 41.8%; p = 0.026)
- lower rate of retreatment (9.9%% vs 22.0%; p = 0.041)
- higher rate of post-embolic syndrome (41.8% vs 8.8%; p<0.001), with no significant differences between groups regarding major adverse events.

Better results for HCC > 3 cm with higher progression free survival

Thus, there is no standard indication.
„Micro-balloon or flow directing microcatheters should be used only in trials". CIRSE academy

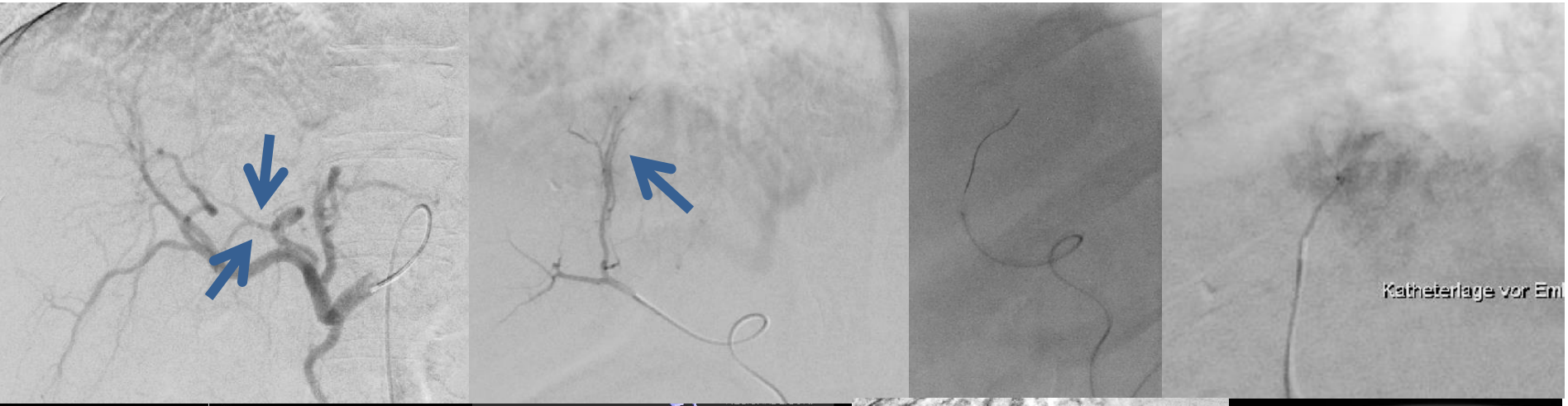
III. Outcomes
Colorectal liver metastases (mCRC)

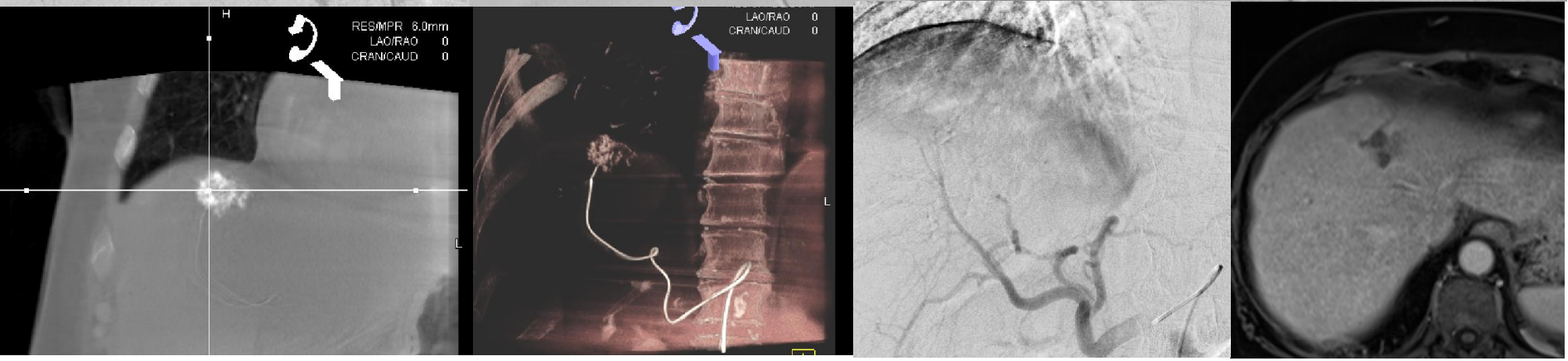
- Carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9) are the markers usually employed in mCRC patients

		1 year survival rate	2 year survival rate	overall survival	median time to progression
Albert et al,2011	mitomycin C, mitomycin C + iritonecan and mitomycin C +gemcitabine cTACE	62%	28%		5 months
Martin et al,2011	55 patients DEM-TACE loaded with irinotecan (DEBIRI)			19 months	11 months
Fiorentini et al,2012	74 patients where DEBIRI- comparison to systemic FOLFIRI DEM-TACE+Irinotecan			22 mo vs 15 mo	22 months
Iezzi et al	20 patients and 54 treatments, DEBIRI + systemic Capecitabine in chemotherapy refractory patients DEM-TACE+Irinotecan+systemic				
Levy et al.	23% cTACE vs. 36% DEM-TACE	70% vs. 80%			
Schicho A et al (2018)	DSM-TACE	objective response 40%, disease control 64.9%			

III. Outcomes
Colorectal liver metastases (mCRC)

CRC, Seg. 4a, DEB TACE, 100mg Irinotecan +HepaSphere 30-60 microns





CBCT (cone beam CT)

III. Outcomes
Intrahepatic cholangiocarcinoma (ICC)

Schicho A, Pereira PL, Haimerl M, et al. (2017) Transarterial chemoembolization (TACE) with degradable starch microspheres (DSM) in hepatocellular carcinoma (HCC): multi-center results on safety and efficacy. Oncotarget, 8(42):72613-72620

Hyder O, Marsh JW, Salem R, et al. (2013) Intra-arterial therapy for advanced intrahepatic cholangiocarcinoma: a multi-institutional analysis. Annals of surgical oncology, 20(12):3779-3786

Labib PL, Davidson BR, Sharma RA, Pereira SP (2017) Locoregional therapies in cholangiocarcinoma. Hepatic oncology, 4(4):99-109

- In ICC clinical outcome data for hepatic arterial perfusion, cTACE and TARE are still controversial.
- Early studies: median OS of 13 months without any difference between cTACE, bland, DEB-TACE and TARE
- more recent reviews: *wider range between 12-25.2 months of OS for TACE and between 14.9-43.7 months for TARE*
- *DSM-TACE: disease control rate in 44% of patients in 7 patients.*
- Consequently, current guidelines do not make any distinct recommendations regarding a specific transarterial treatment.

III. Outcomes
Neuroendocrine tumour (NET)

Da Dong X, Carr BI (2011) Hepatic artery chemoembolization for the treatment of liver metastases from neuroendocrine tumors: a long-term follow-up in 123 patients. Medical Oncology, 28(1):286-290

- *cTACE,* the median overall survival ranges from 24 to 44 months,
- 192 patients overall survival rate of 36% at 5 years, retrospective report

Do Minh D, Chapiro J, Gorodetski B, et al. (2017) Intra-arterial therapy of neuroendocrine tumour liver metastases: comparing conventional TACE, drug-eluting beads TACE and yttrium-90 radioembolisation as treatment options using a propensity score analysis model. Eur Radiol, 27(12):4995-5005

- 123 patients:significantly longer *median overall survival for cTACE (33.8 months) compared with DEM-TACE (21.7 months, p <.01*) or Y90 (23.6 months, p = 0.02), remains unclear which patient-specific parameters might explain these results.

- For NETs, the commonly used serum markers are neuron specific enolase (NSE) and chromogranin A

III. Outcomes
Procedure specific complications

Filippiadis DK, Binkert C, Pellerin O, Hoffmann RT, Krajina A, Pereira PL (2017) Cirse Quality Assurance Document and Standards for Classification of Complications: The Cirse Classification System. Cardiovascular and interventional radiology, 40(8):1141-1146

Gaba RC, Lokken RP, Hickey RM, et al. (2017) Quality Improvement Guidelines for Transarterial Chemoembolization and Embolization of Hepatic Malignancy. Journal of vascular and interventional radiology : JVIR, 28(9):1210-1223 e1213

- Complications in the context of TACE occur in about 10 % of cases
- *intraprocedural* (e.g. catheter/guidewire induced vascular injury or haemorrhage, immediate vascular thrombosis, aberrant embolisation)
- *periprocedural* (metabolic impairment), delayed (e.g. liver failure, peribiliary necrosis)
- *minor and major* (all events as abscess, bilioma, haemorrhage, liver failure, vascular damage that need some kind of intervention)

III. Outcomes
Procedure specific complications

Post embolisation syndrome (PES):

- is not considered a complication and is expected in about 30 % of cases as an effect of an efficient chemoembolisation.
- usually self-limiting and should last only a few days within the first two weeks after the procedure.
- nausea, vomiting, fever, pain, and fatigue necessitating no or only symptomatic treatment.
- In rare, cases it may last up to four weeks post TACE. Longer lasting symptoms should prompt evaluation for other causes.

III. Outcomes
Procedure specific complications

- *Vascular complications* as haemorrhage, dissection or pseudoaneurysm of the celiac trunk or hepatic artery are rare and should whenever possible be treated by interventional techniques.
- *Infectious conditions,* such as cholangitis, cholecystitis, but also initial abscesses, infected hemangiomas or bilomas are initially treated using antibiotics. In liquified infected fluid collections, percutaneous drainage is appropriate and a surgical intervention may be necessary in rare cases.

III. Outcomes-Imaging follow-up

HCC and mCRC

Lencioni R, Llovet JM. Modified RECIST (mRECIST) assessment for hepatocellular carcinoma. Semin Liver Dis. 2010 Feb;30(1):52-60.

Table 2 Assessment of Target Lesion Response: Conventional RECIST and mRECIST Assessment for HCC Following the AASLD-JNCI Guideline

mRECIST for HCC
CR = Disappearance of any intratumoral arterial enhancement in all target lesions
PR = At least a 30% decrease in the sum of diameters of viable (enhancement in the arterial phase) target lesions, taking as reference the baseline sum of the diameters of target lesions
SD = Any cases that do not qualify for either partial response or progressive disease
PD = An increase of at least 20% in the sum of the diameters of viable (enhancing) target lesions, taking as reference the smallest sum of the diameters of viable (enhancing) target lesions recorded since treatment started

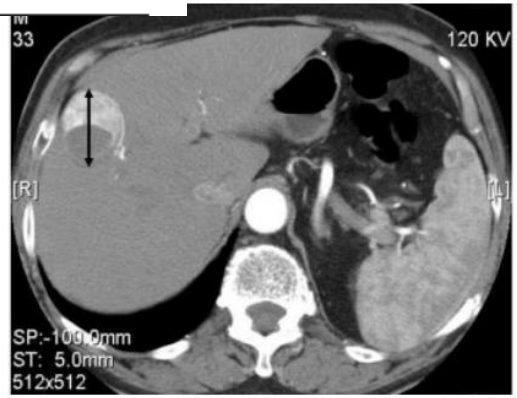
HCC: mRECIST:

Measurement of longest viable tumor diameter

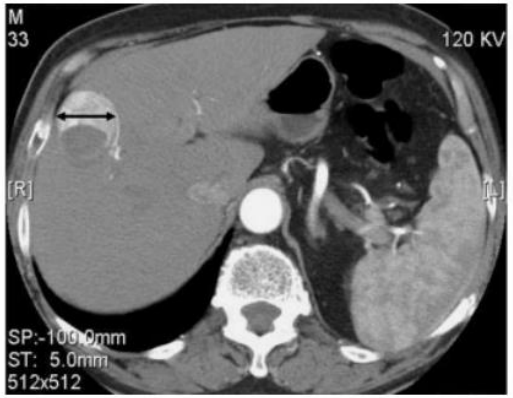
mCRC: RECIST version 1.1

Measurement of longest overall tumor diameter according to conventional RECIST

conventional RECIST



mRECIST



III. Outcomes-Imaging follow-up

Kudo, M.; Han, K.H.; Ye, S.L.; Zhou, J.; Huang, Y.H.; Lin, S.M.; Wang, C.K.; Ikeda, M.; Chan, S.T.; Choo, S.P.; et al. A changing paradigm for the treatment of intermediate-stage hepatocellular carcinoma: Asia-Pacific Primary Liver Cancer Expert Consensus Statements. Liver Cancer 2020, 9, 245–260.

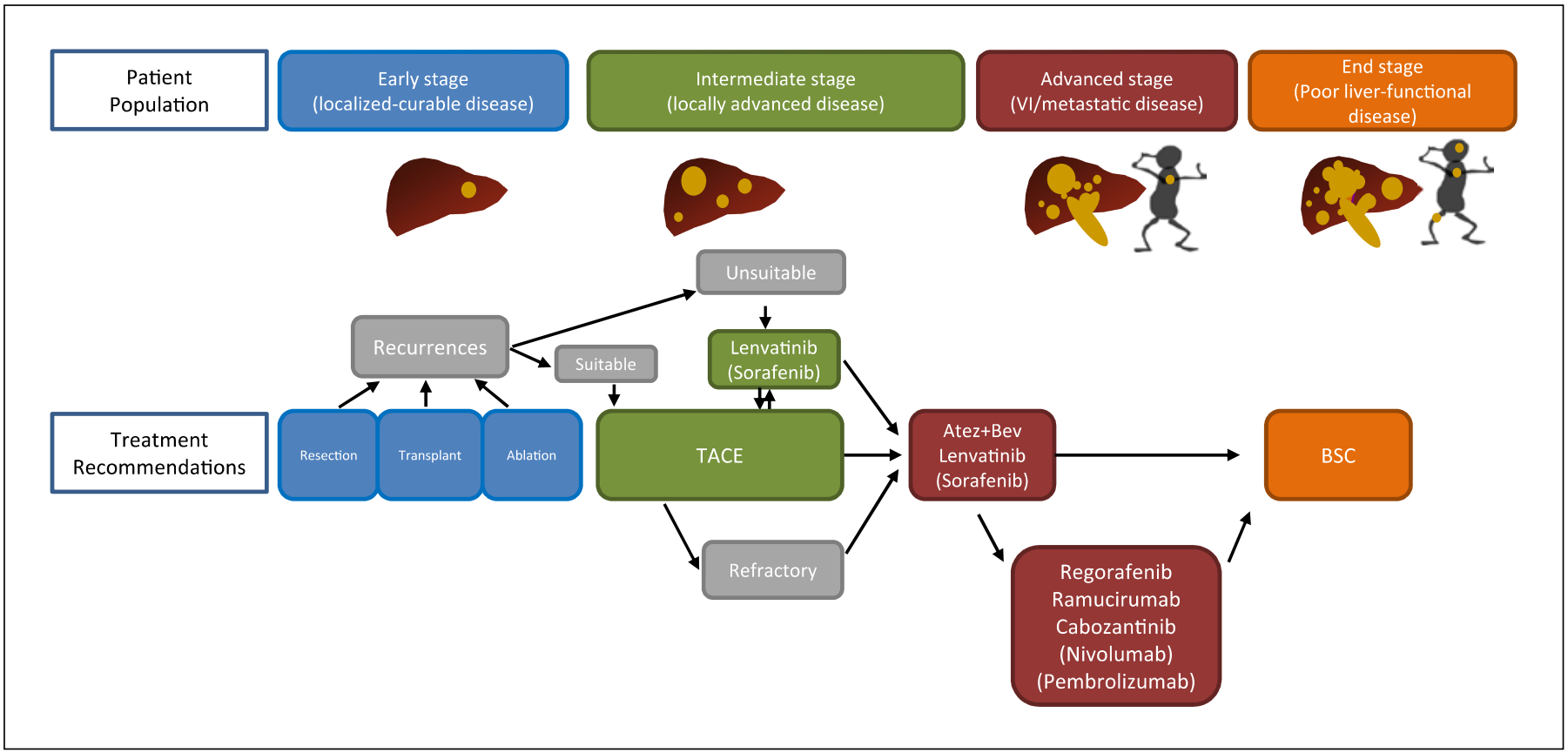


Fig. 4. A new paradigm for treatment strategy in HCC. For patients who are unsuitable to TACE, systemic therapy using agents with a high response rate followed by selective TACE would be a better treatment strategy to prolong patients' survival. TACE, transarterial chemoembolization.

III. Outcomes
Re-TACE planning and scoring systems

identify poor candidates before the first treatment session

Kadalayil L, Benini R, Pallan L, et al. (2013) A simple prognostic scoring system for patients receiving transarterial embolisation for hepatocellular cancer. Annals of oncology : official journal of the European Society for Medical Oncology, 24(10):2565-2570

- HAP score

Table 3. Calculation of the Hepatoma arterial-embolisation prognostic (HAP) score

Prognostic factor	Points
Albumin < 36 g/dl	1
AFP > 400 ng/ml	1
Bilirubin > 17 µmol/l	1
Maximum tumour diameter >7 cm	1
HAP classification	Points
HAP A	0
HAP B	1
HAP C	2
HAP D	>2

Hucke F, Pinter M, Graziadei I, et al. (2014) How to STATE suitability and START transarterial chemoembolization in patients with intermediate stage hepatocellular carcinoma. Journal of hepatology, 61(6):1287-1296

- STATE score

The STATE-score starts with the serum-albumin level (g/L), which is reduced by 12 points each, if the tumour load exceeds the up-to-7 criteria and/or C-reactive protein (CRP) levels are P1 mg/dl (maximum reduction: 24 points).

Up-to-7 in/beyond: the size of the largest tumour nodule and the number of all nodules is smaller/ greater than seven.

Table 3. Results of multivariable stepwise backward Cox regression analysis of prognostic factors in patients with HCC treated with transarterial (chemo)embolization in the training cohort.

		Overall survival			STATE-score	*p* value
Variable		HR	95% CI	B	Points	(Cox regression)
Up-to-seven	In	1			0	
	Beyond	2.2	1.4-3.4	0.779	-12	0.001
Albumin	g/L	0.94	0.8-1.0	-0.066	ALBUMIN-value	0.005
CRP-values	<1 mg/dl	1			0	
	≥1 mg/dl	2.2	1.4-3.6	0.798	-12	0.001

III. Outcomes
Re-TACE planning and scoring systems

The ART score aims to assess retreatment

- ART score

Sieghart W, Hucke F, Pinter M, Graziadei I, Vogel W, Müller C, Heinzl H, Trauner M, Peck-Radosavljevic M. The ART of decision making: retreatment with transarterial chemoembolization in patients with hepatocellular carcinoma. Hepatology. 2013 Jun;57(6):2261-73.

Table 3. Results of Multivariate Stepwise Backward Cox Regression Analysis of Prognostic Factors in Patients With HCC Treated With TACE in the Training Cohort

Variable		Overall Survival HR	95% CI	B	ART Score Points*	*P*-value (Cox Regression)
Child-Pugh score increase	Absent	1			–	
	+ 1 point	2.0	1.2-3.5	0.71	1.5	
	+ ≥2 points	4.4	2.0-9.6	1.49	3	<0.001
AST increase >25%	Absent	1			–	
	Present	8.4	4.5-15.5	2.13	4	<0.001
Radiologic tumor response	Present	1			–	
	Absent	1.7	1.1-2.6	0.51	1	0.026

Abbreviations: HCC, hepatocellular carcinoma; AST, aspartate aminotransferase.
*The regression coefficients (B) were multiplied by 2 and rounded in order to facilitate the bedside calculation of the ART score.

An ART score of >= 2.5 prior the second TACE identifies patients with a dismal prognosis who may not profit from further TACE sessions.

Digestive Diseases

Original Article

Dig Dis 2014;32:711–716
DOI: 10.1159/000368007

The ART Score Is Not Effective to Select Patients for Transarterial Chemoembolization Retreatment in an Italian Series

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The ART score was not found to work as an objective tool to guide TACE retreatment in our Italian patient series, only the Child-Pugh score increase was an independent predictor of a shorter survival.

III. Outcomes
Re-TACE planning and scoring systems

"untreatable progression"

- TACE should not be repeated when substantial necrosis is not achieved after two rounds of treatment
- follow-up treatment fails to induce marked necrosis at sites that have progressed after an initial tumour response.
- TACE should not be repeated in patients with tumour progression associated with a clinical profile that prevents re-treatment, e.g. development of liver failure.
- extensive liver involvement, extrahepatic metastasis or vascular invasion, but also minor intrahepatic progression associated with impaired liver function and performance status

IV. Future perspectives: New drugs-Triple-drug

Shi M, Lu LG, Fang WQ, et al. (2013) Roles played by chemolipiodolization and embolization in chemoembolization for hepatocellular carcinoma: single-blind, randomized trial. Journal of the National Cancer Institute, 105(1):59-68

- 365 patients
- Lobaplatin+epirubicin+mitomycin C: OS benefit as compared to single-drug (epirubicin) TACE
- Survival was statistically significantly better in Arm 1 than in Arm 3 ($P < .001$), whereas there was no statistically significant difference between Arm 1 and Arm 2 ($P = .20$).

triple-drug chemolipiodolization with embolization (Arm 1)
triple-drug chemolipiodolization without embolization (Arm 2)
single-drug chemolipiodolization with embolization (Arm 3)

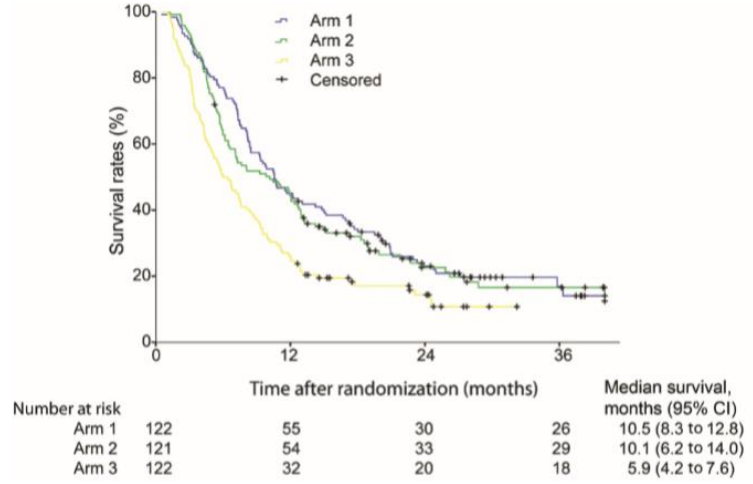
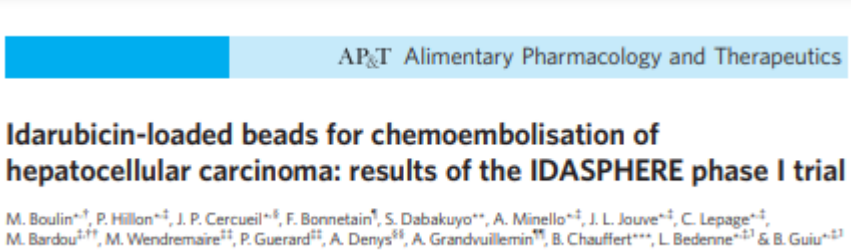


Figure 2. Kaplan–Meier estimated curves of patients with unresectable hepatocellular carcinoma, stratified based on transarterial chemoembolization allocation, including triple-drug chemolipiodolization with embolization (Arm 1), triple-drug chemolipiodolization without embolization (Arm 2), and single-drug chemolipiodolization with embolization (Arm 3). CI = confidence interval.

IV. Future perspectives: New drugs-Idarubicin



Alimentary pharmacology & therapeutics, 39(11):1301-1313

- *HCC TACE cytotoxicity study*
- most cytotoxic agent for hepatocellular carcinoma (HCC) cell lines
- Good safety profile and promising clinical efficacy has been reported either for idarubicin cTACE, DEM-TACE or chemolipiodolisation.

No prospective randomised data are available so far.

IV. Future perspectives: New drugs-Idarubicin

- 46 study participants
- Median progression-free survival:6.6 months, time to progression: 9.5 months, overall survival:18.6 months
- TACE was discontinued for toxicity in 9% participants.

Most frequent grade 3-4 adverse events:

- elevated aspartate aminotransferase (14 of 44, 32%)
- elevated γ-glutamyl transpeptidase (eight of 44, 18%)
- hyperbilirubinemia (seven of 44, 16%),
- elevated alanine aminotransferase (seven of 44, 16%)
- pain (seven of 44, 16%).

Radiology

ORIGINAL RESEARCH • VASCULAR AND INTERVENTIONAL RADIOLO

Idarubicin-loaded Beads for Chemoembolization of Hepatocellular Carcinoma: The IDASPHERE II Single-Arm Phase II Trial

Boris Guiu, MD, PhD • Patrick Chevallier, MD, PhD • Eric Assenat, MD, PhD • Emilie Barbier, PhD • Philippe Merle, MD, PhD • Antoine Bouvier, MD • Jérôme Dumortier, MD, PhD • Eric Nguyen-Khac, MD • Jean Gugenheim, MD, PhD • Agnès Rode, MD • Frédéric Oberti, MD • Pierre-Jean Valette, MD, PhD • Thierry Yzet, MD • Olivier Chevallier, MD • Jean-Claude Barbare, MD • Marianne Latournerie, MD • Mathieu Boulin, PharmD, PhD

Radiology. 2019 Jun;291(3):801-808.

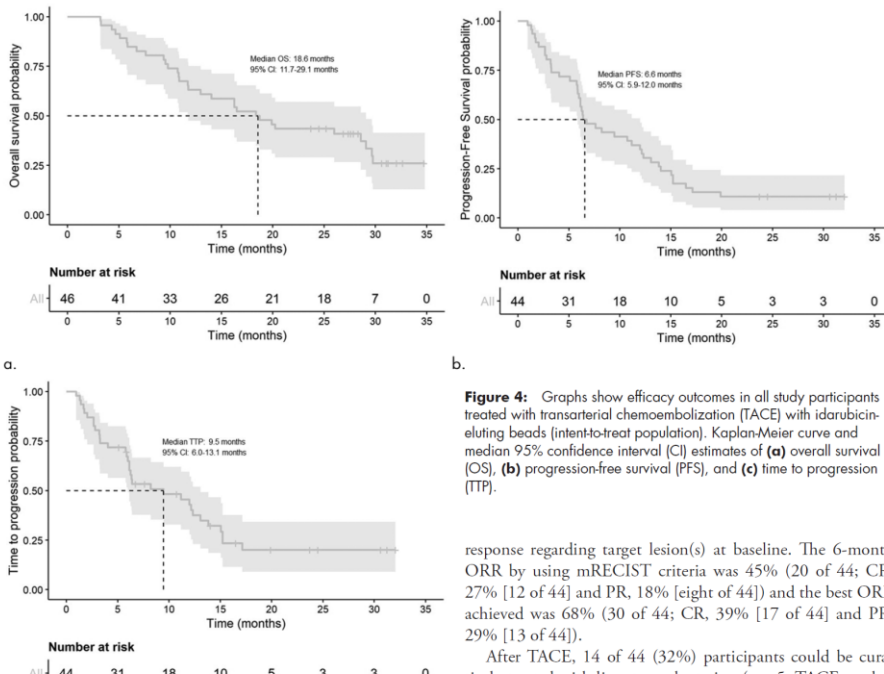


Figure 4: Graphs show efficacy outcomes in all study participants treated with transarterial chemoembolization (TACE) with idarubicin-eluting beads (intent-to-treat population). Kaplan-Meier curve and median 95% confidence interval (CI) estimates of **(a)** overall survival (OS), **(b)** progression-free survival (PFS), and **(c)** time to progression (TTP).

response regarding target lesion(s) at baseline. The 6-mont
ORR by using mRECIST criteria was 45% (20 of 44; CI
27% [12 of 44] and PR, 18% [eight of 44]) and the best OR
achieved was 68% (30 of 44; CR, 39% [17 of 44] and PR
29% [13 of 44]).

After TACE, 14 of 44 (32%) participants could be cura
tively treated with liver transplantation (n = 5; TACE used a
bridging therapy [n = 3] or as downstaging strategy [n = 2]
percutaneous thermal ablation (n = 6), or resection (n = 3

IV. Future perspectives: TACE plus systemic therapies

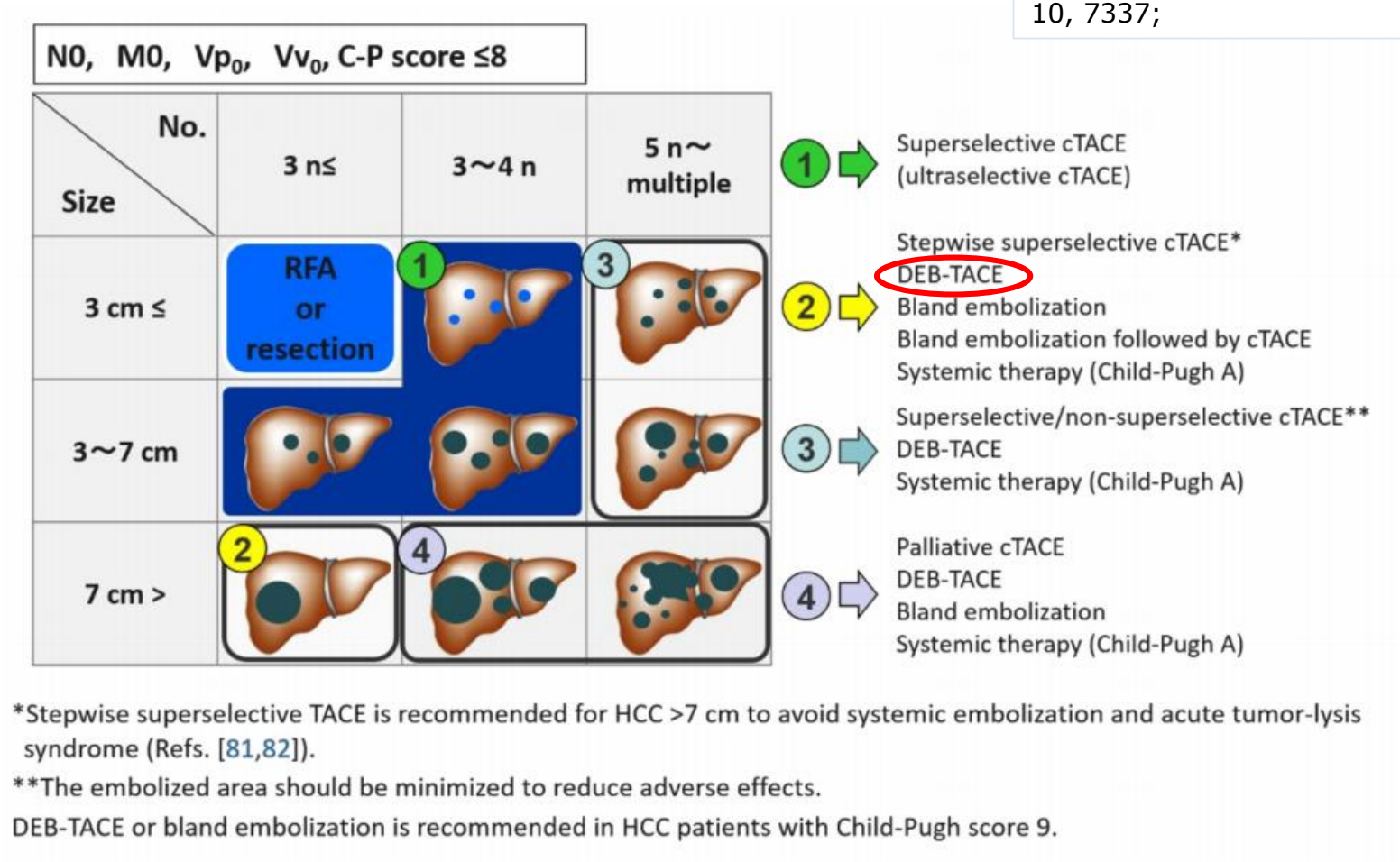
Llovet JM, Kelley RK, Villanueva A, et al. (2021) Hepatocellular carcinoma. Nature Reviews Disease Primers, 7(1):6

- **Combining targeted therapies +TACE:**
  - *SPACE, TACE 2* and *TACTICS trials*: sorafenib, BRISK-TA trial: brivanib *ORIENTAL trial*: orantinib
  - No OS improvement
- **Combining anti-angiogenic molecules +TACE:**
  - Only *TACTICS trial* (comparing TACE to sorafenib-TACE-sorafenib (interruption for 2 days before and after TACE) benefit in

    PFS (25.2 vs. 13.5 months; p=0.006),
  - all combination trials with tyrosine-kinase inhibitors or anti-angiogenics were all negative
- **Immunotherapy:** combination of various immune-checkpoint inhibitors, alone or in combination with TACE
  - *EMERALD-1 trial*: durvalumab + bevacizumab
  - *TACE-3 trial:* nivolumab,
  - *LEAP-012 trial:* Lenvatinib+pembrolizumab,
  - *CheckMate 74W trial:* nivolumab + ipilimumab.
  - The results of these phase III randomised trials are pending and might define new standards in the future

Our TACE strategy according to the patient and tumor conditions

Treatment Strategy of Transarterial Chemoembolization for Hepatocellular Carcinoma Shiro MiyayamaAppl. Sci. 2020, 10, 7337;



*Stepwise superselective TACE is recommended for HCC >7 cm to avoid systemic embolization and acute tumor-lysis syndrome (Refs. [81,82]).

**The embolized area should be minimized to reduce adverse effects.

DEB-TACE or bland embolization is recommended in HCC patients with Child-Pugh score 9.

Thank you for your attention