

# **Neue Embolisationsmaterialien**

## **DCBeads & Co.**

### **Prof. Dr. Philippe L. Pereira**

**Professor of Radiology and Research Director  
Chairman of the Clinic of Radiology, Minimally Invasive Therapies and Nuclearmedicine**

**SLK-Clinics Heilbronn**

**Ruprecht-Karls-University of Heidelberg,**

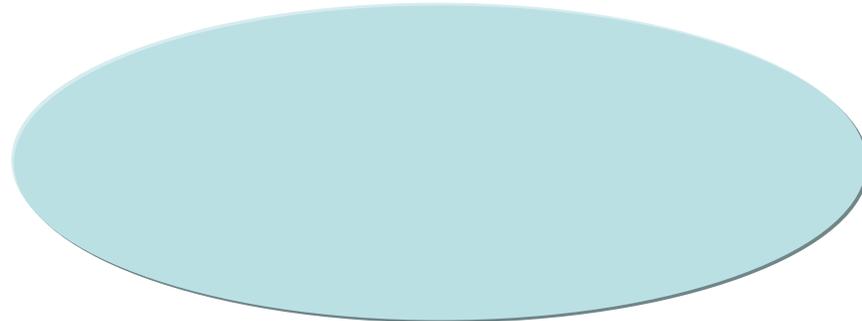
**Eberhard-Karls University of Tübingen, Germany**

*Philippe.pereira@slk-kliniken.de*

# Embolization

## major clinical indications

1. Arteriovenous malformations (AVMs)
2. Hypervascularized tumors  
(**liver tumors**, head & neck tumors,  
uterus fibroids and prior to surgery)
3. Bleedings



# New embolization in liver diseases

## Current knowledges and hypothesis

1. Similar to worldwide experience has supported the use of curative RFA and surgery for **HCC<3cm** with 3-year disease control rate up to 90%
2. Classical TACE: No evidence EBM-A of efficacy in **liver metastastic diseases**
3. For **intermediate-stage HCC** (multinodular or >3cm) **chemoembolization or embolization** have been the default ttt option (palliative option)

# “Alte” Embolisation:

## Variationen

- anticancer drug(s) used
- dosage of chemotherapeutic agent
- treatment schedule
- use of lipiodol
- embolising agent
- delivery and timing
- selectivity (amount of liver embolised)

# Systematische Review der Leberembolisation

## Welches Embolisat?

- In 52 studies of TACE or TAE, gelatin sponge was the most common embolising agent
  - gelatin sponge: 71%
  - polyvinyl alcohol particles: 8%
  - degradable starch microspheres: 4%
  - trisacryl gelatin microspheres: 4%
  - surgical ligation: 2%
  - autologous blood clot: 2%
  - not reported: 11%
- **Conclusion**
  - **there is no consensus regarding the most effective embolising agent**

# .....Neue Embolisate & Liver Tumor

## 1. DC Beads®:

medikamentenfreisetzende Partikel

## 2. Embozene®, HepaSpher®: blande Embolisation

## 3. Gelpart®: *gelatine particle 1,000µ, extremely diluted for bland embolization*

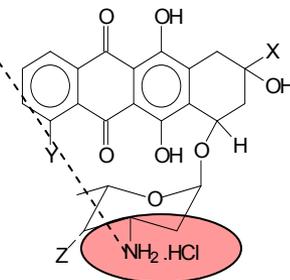
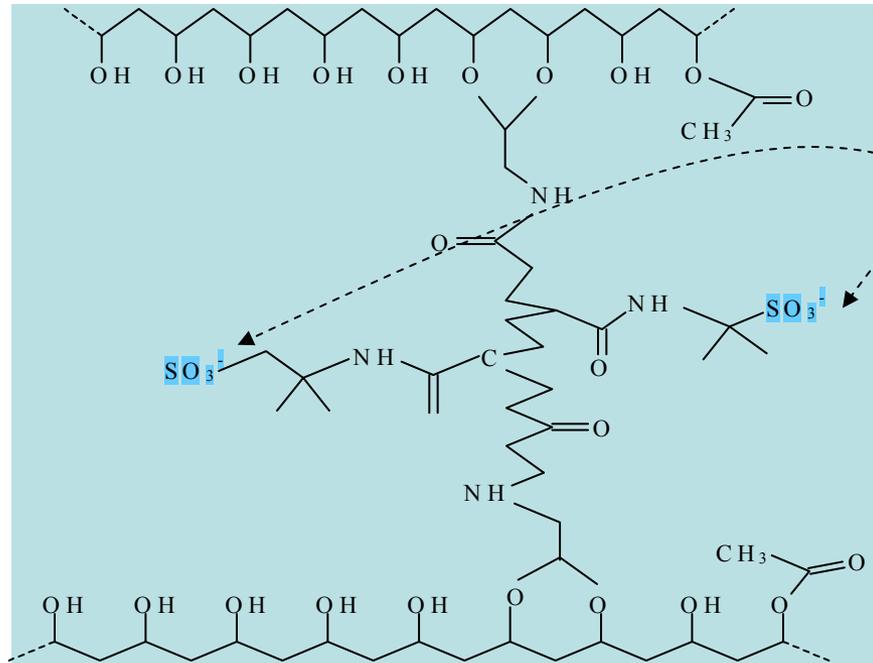
# Bead block for embolization

Partikel: 100-1,200 $\mu$

100 - 300 $\mu$ m		Meningioma, glomus tumours, AVM's liver tumours, chemoembolization
300 - 500 $\mu$ m		Epistaxis, bleeding, AVM's, chemoembolization, paraganglioma
500 - 700 $\mu$ m		UFE paraganglioma, epistaxis
700 - 900 $\mu$ m		UFE, renal tumours
900 - 1200 $\mu$ m		UFE

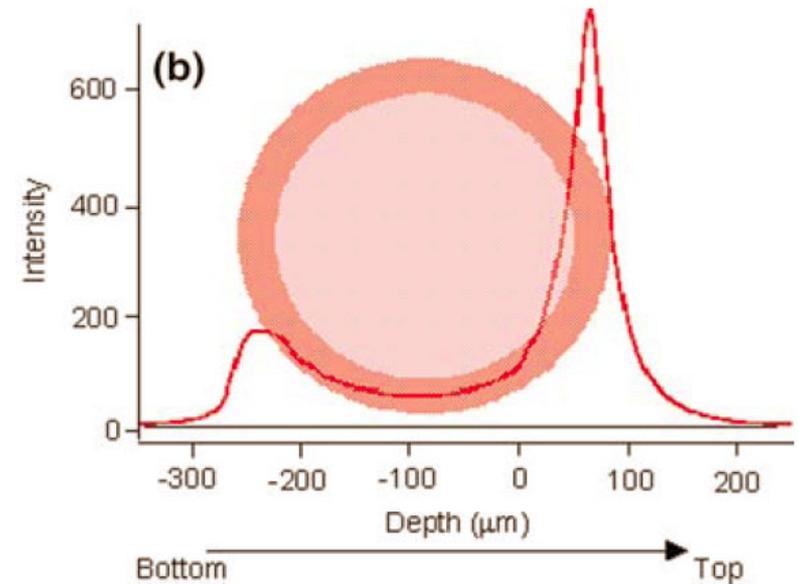
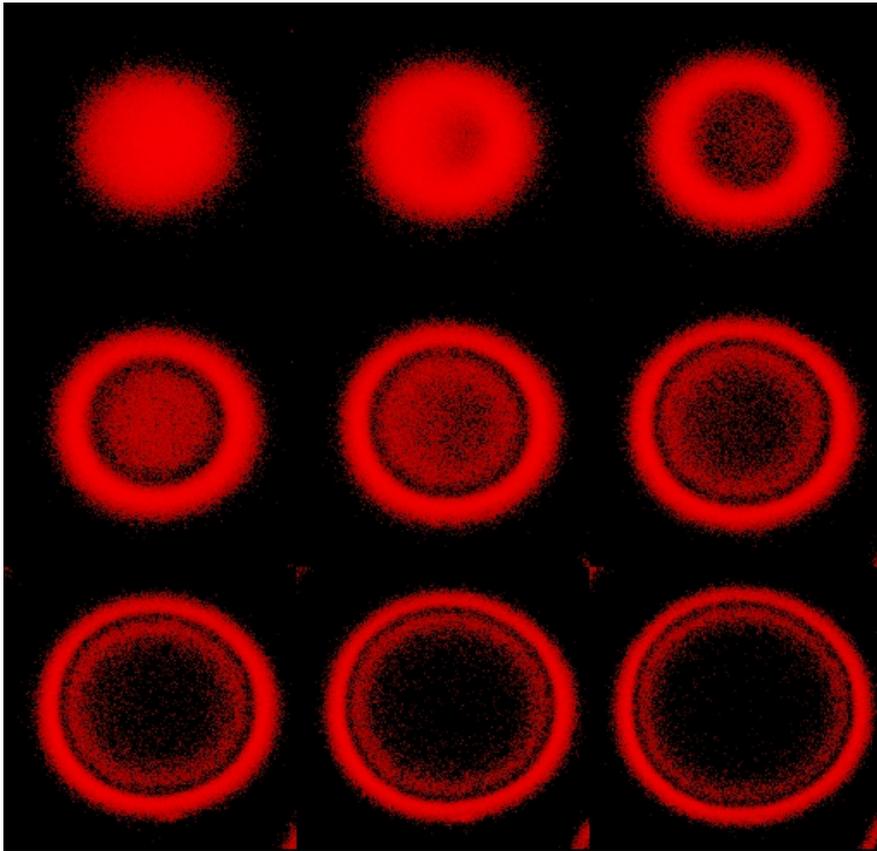
# Bead block für Embolisation

Partikel: 100-1,200 $\mu$

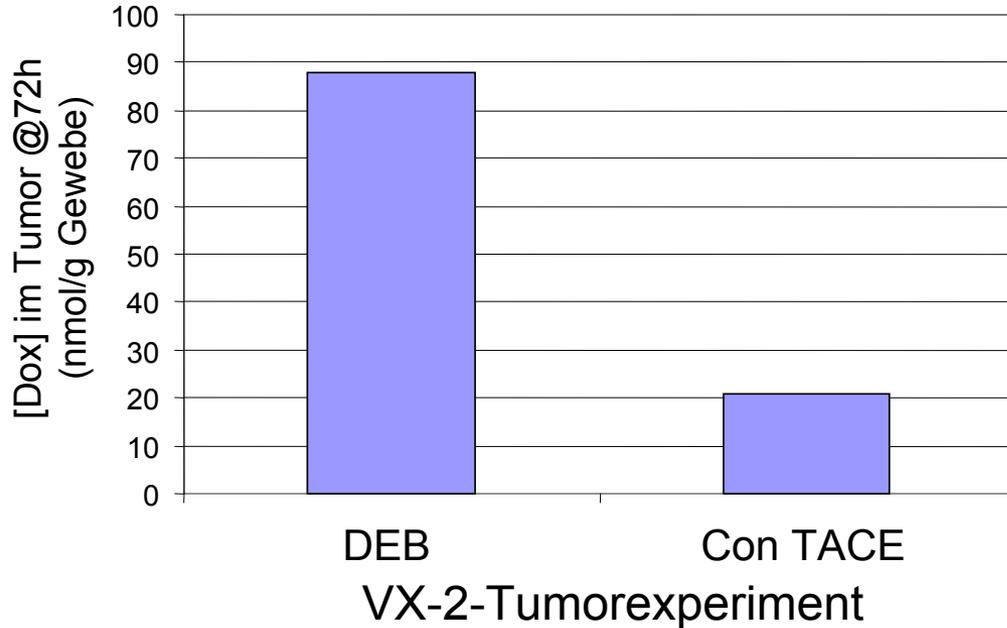


Doxorubicin

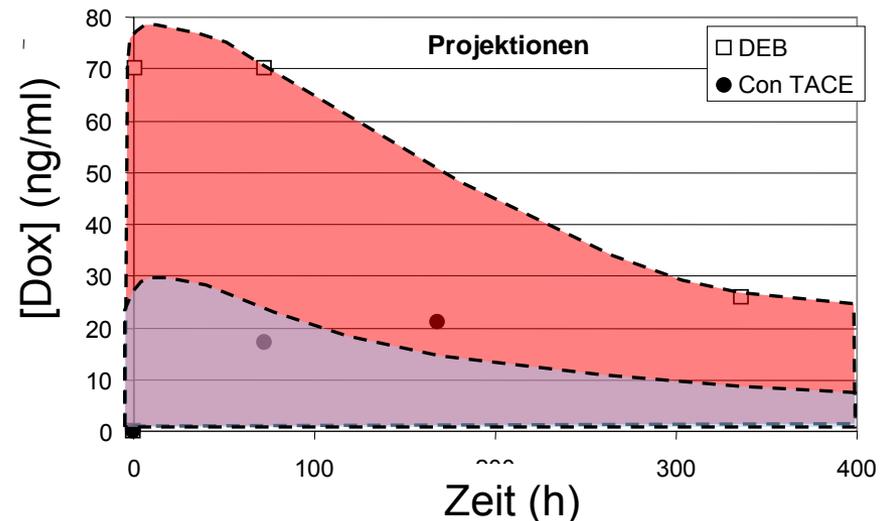
# Lokalisation von Doxorubicin in den Partikeln: DC Beads



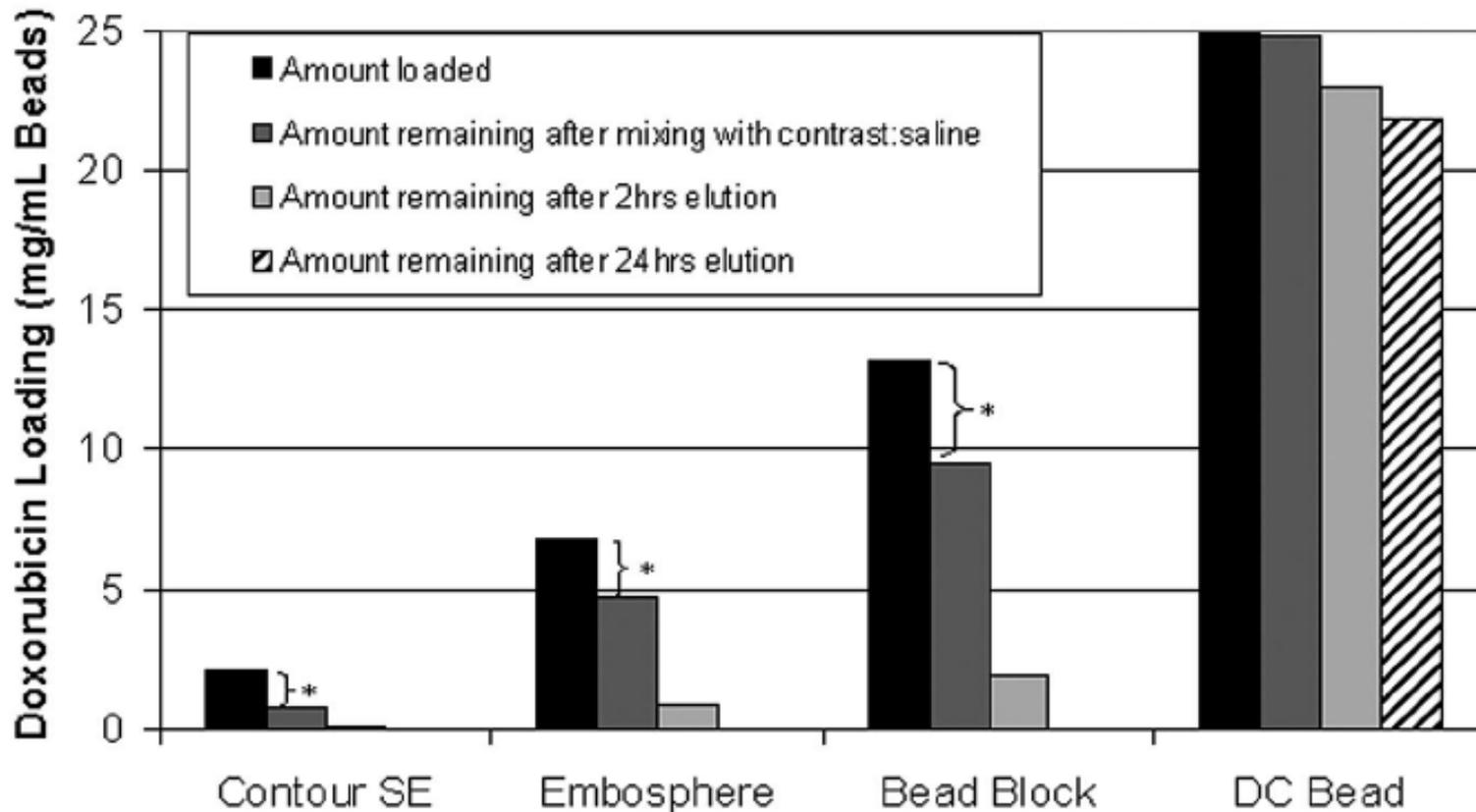
# Höhere Konzentration von Doxorubicin im Tumor



*Ca. 400% mehr Doxorubicin im Tumor mit DEB*

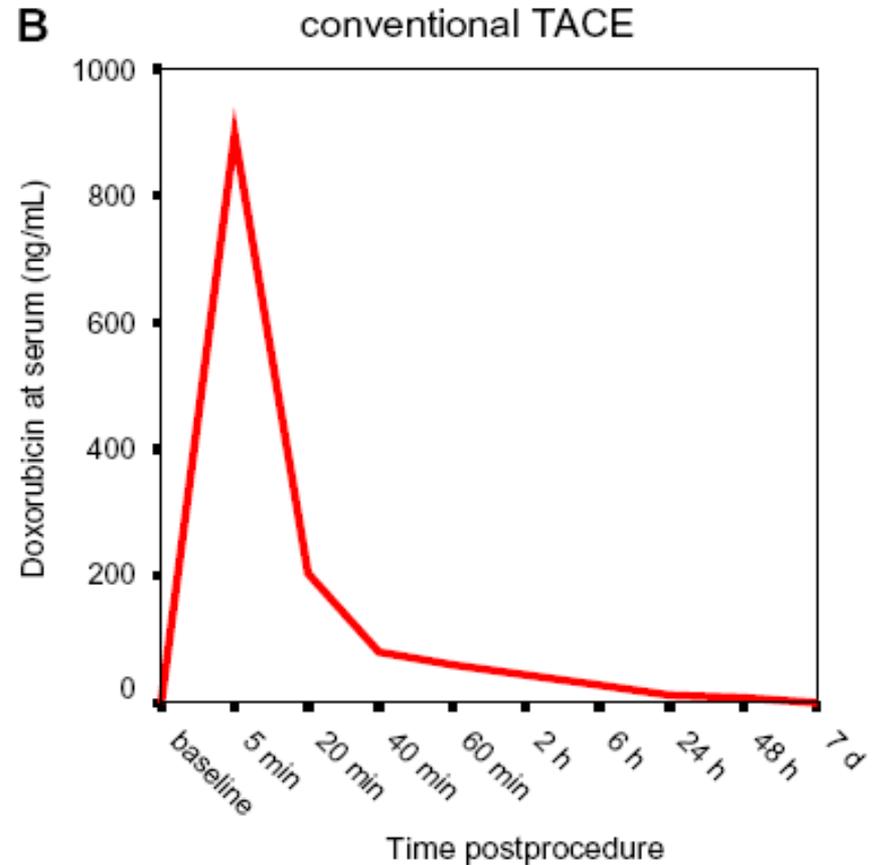
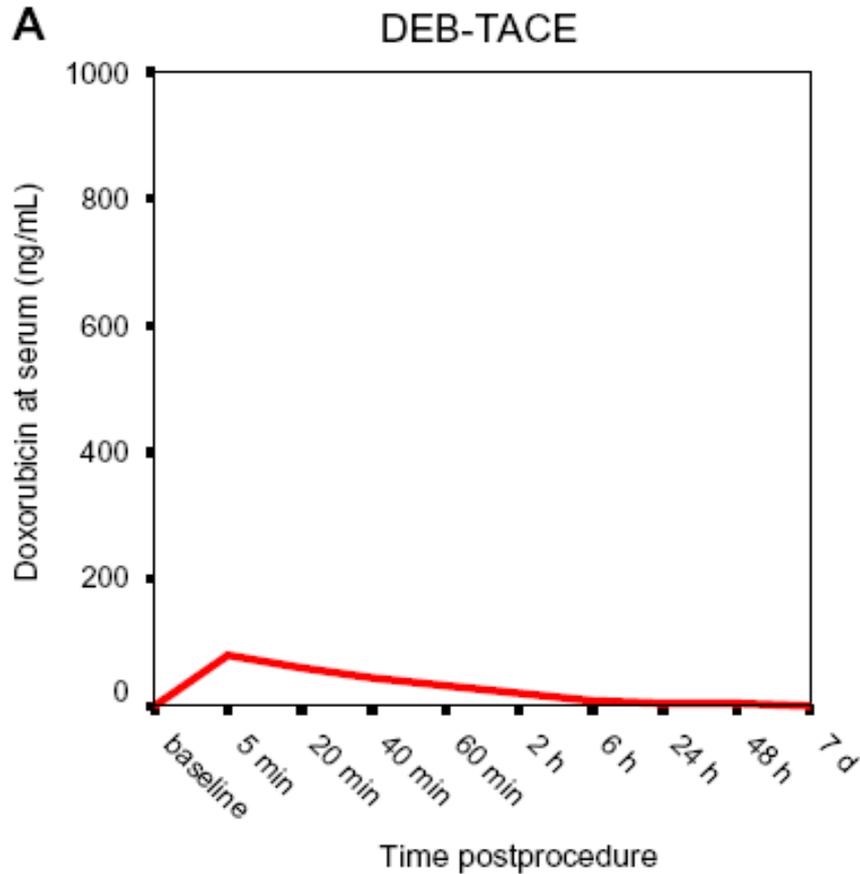


# Vergleich nach Beladung verschiedener Partikel



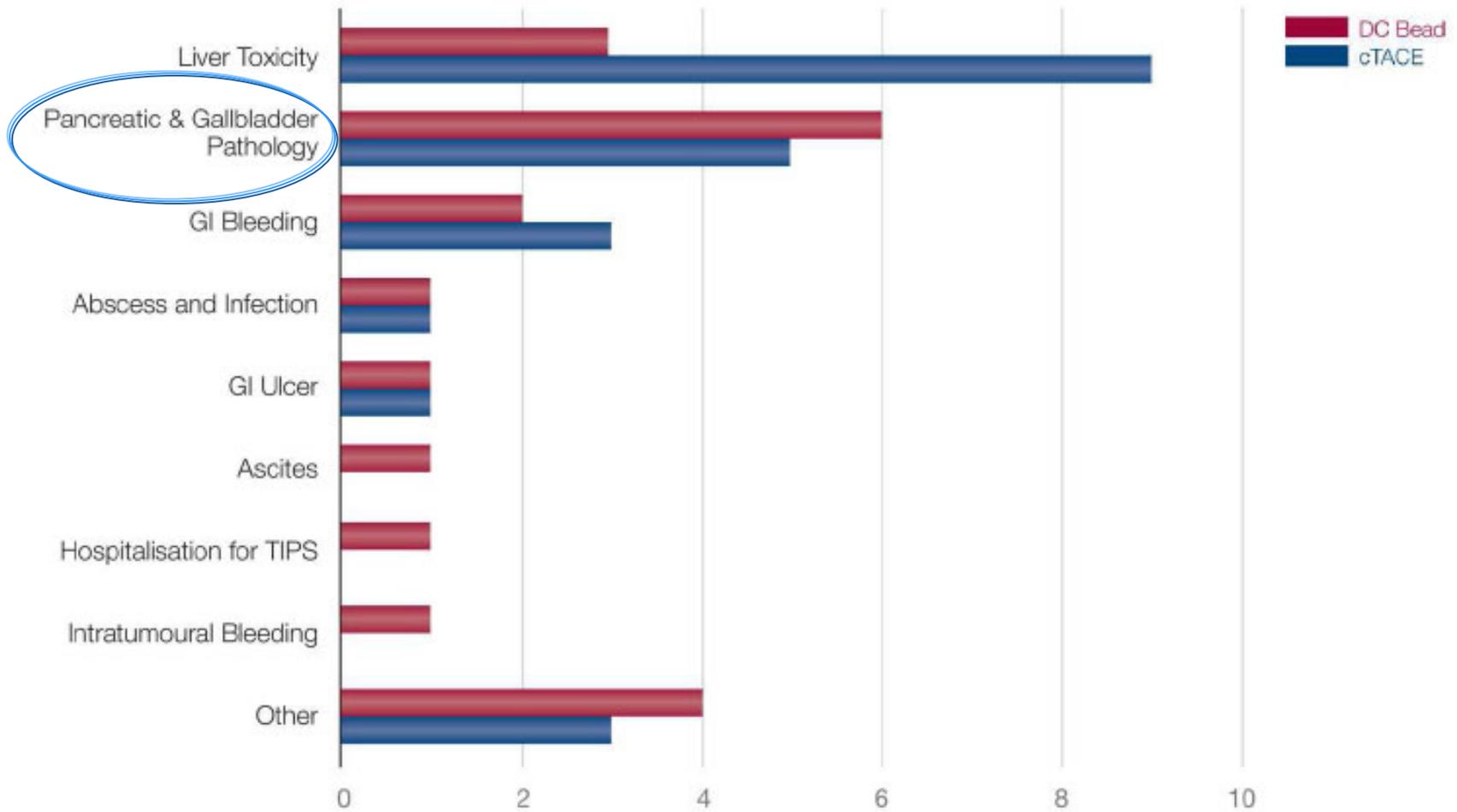
# Systemische Doxorubicin-Konzentrationen: DC Beads

27 Pat. DEB-TACE, 5 konvent. TACE, prospektiv



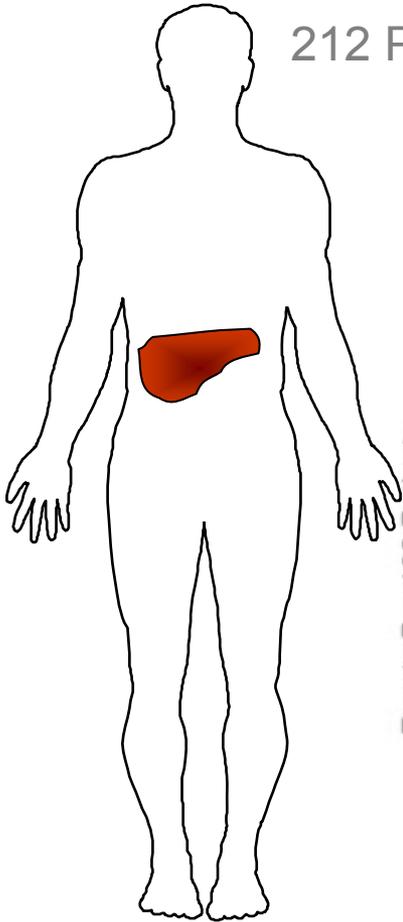
# Precision V: Gastrointestinale SAEs

212 Patienten (DC-Bead 102, cTACE 110), multicentr. RCT

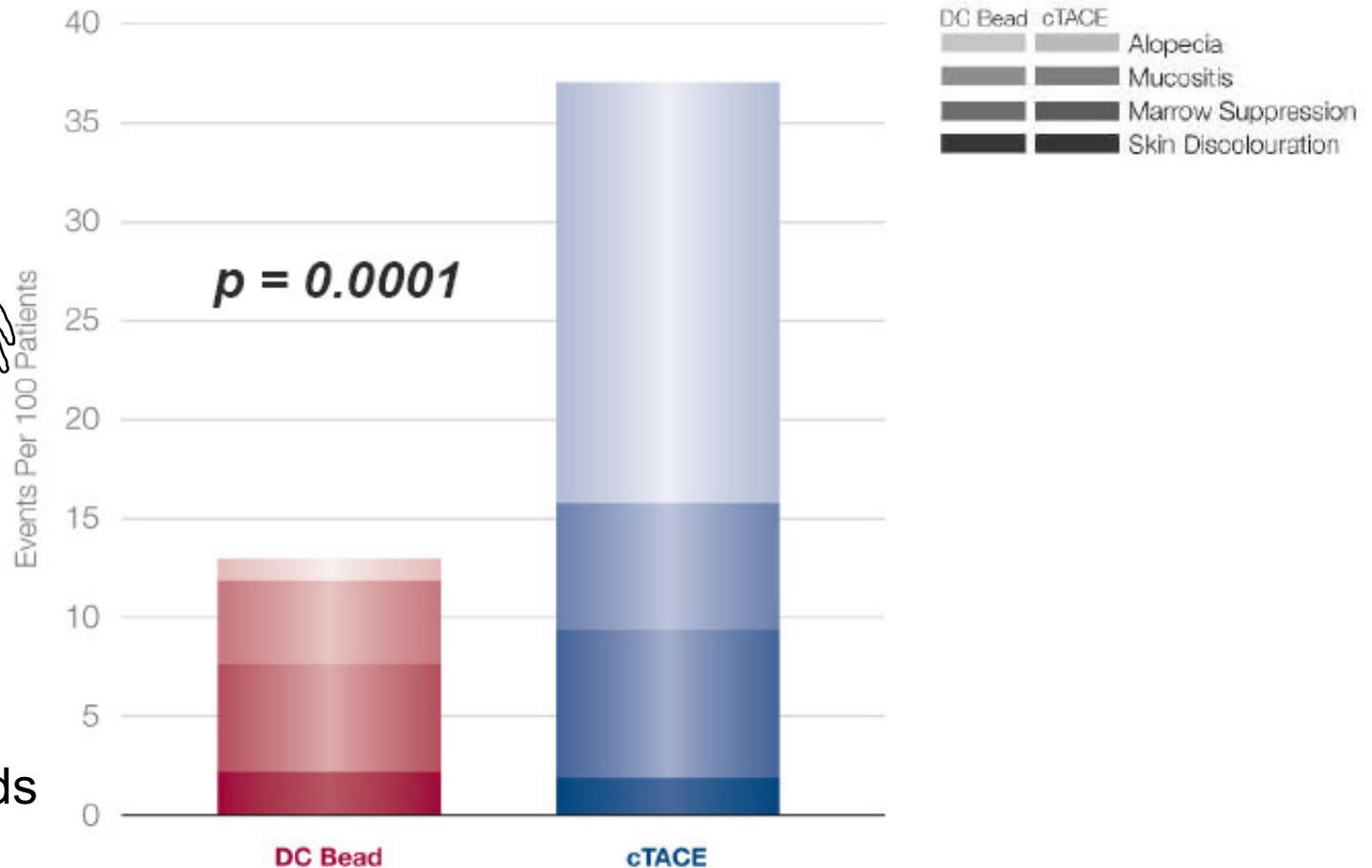


# Precision V: Doxorubicin-Nebenwirkungen

212 Patienten (DC-Bead 102, cTACE 110), multicentr. RCT



Drug eluting Beads



# Precision V:

## Tumorrespons nach 6 Monaten

212 Patienten (DC-Bead 102, cTACE 110), multicentr. RCT



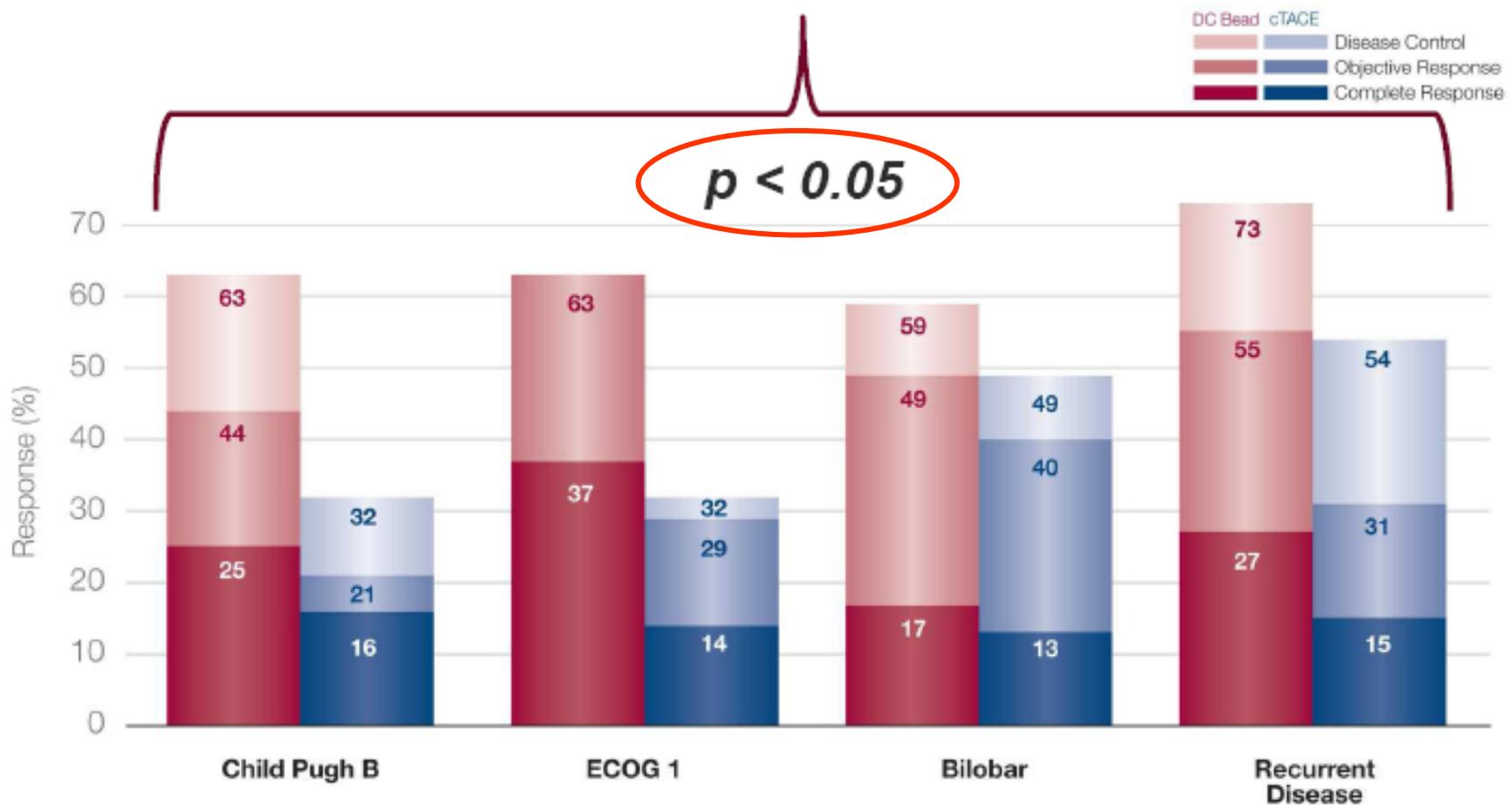
Disease Control = Objective Response + Stable Disease

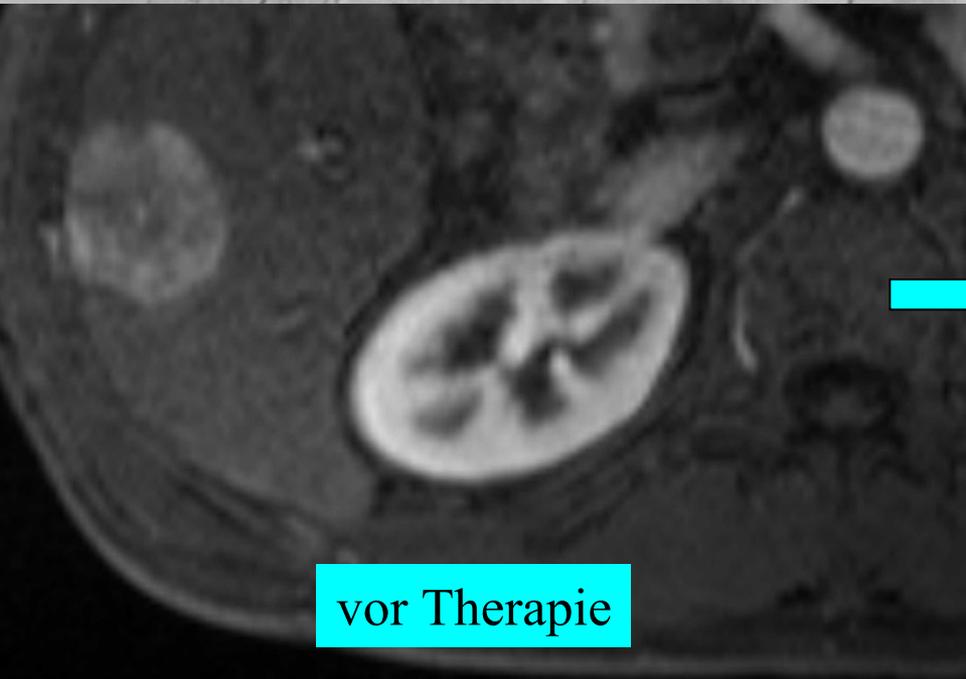
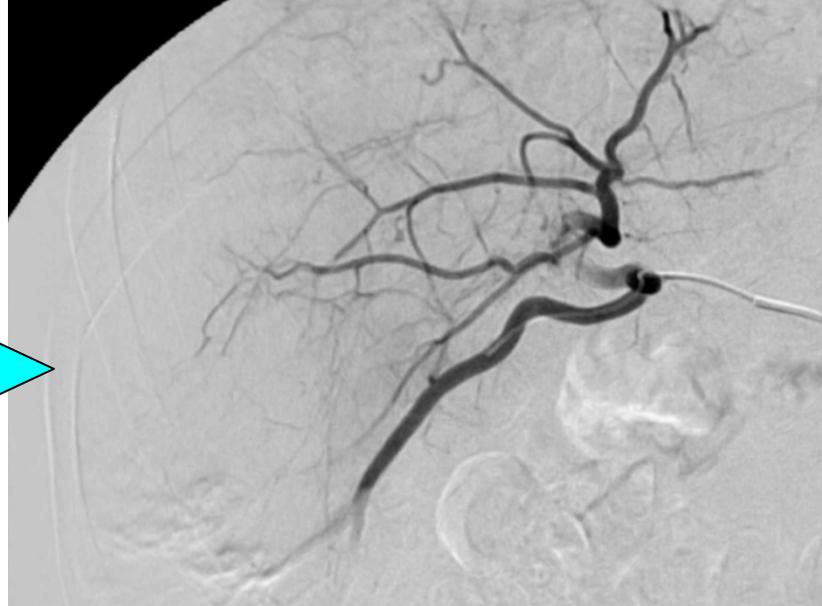
Objective Response = Complete Response + Partial Response

# Precision V:

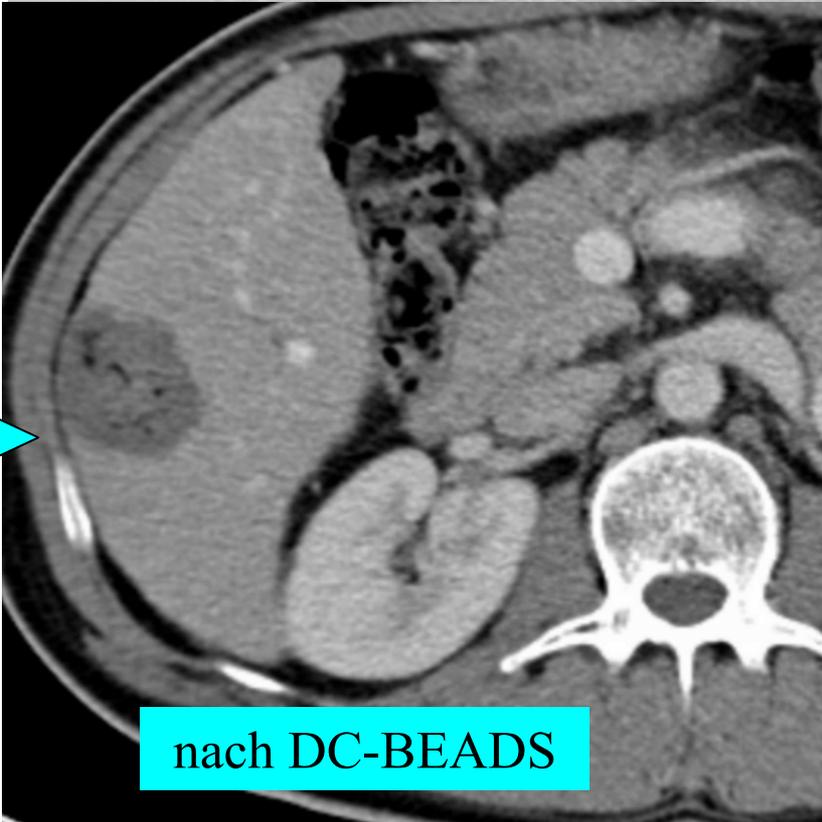
## Tumorrespons nach 6 Monaten

212 Patienten (DC-Bead 102, cTACE 110), multicentr. RCT





vor Therapie

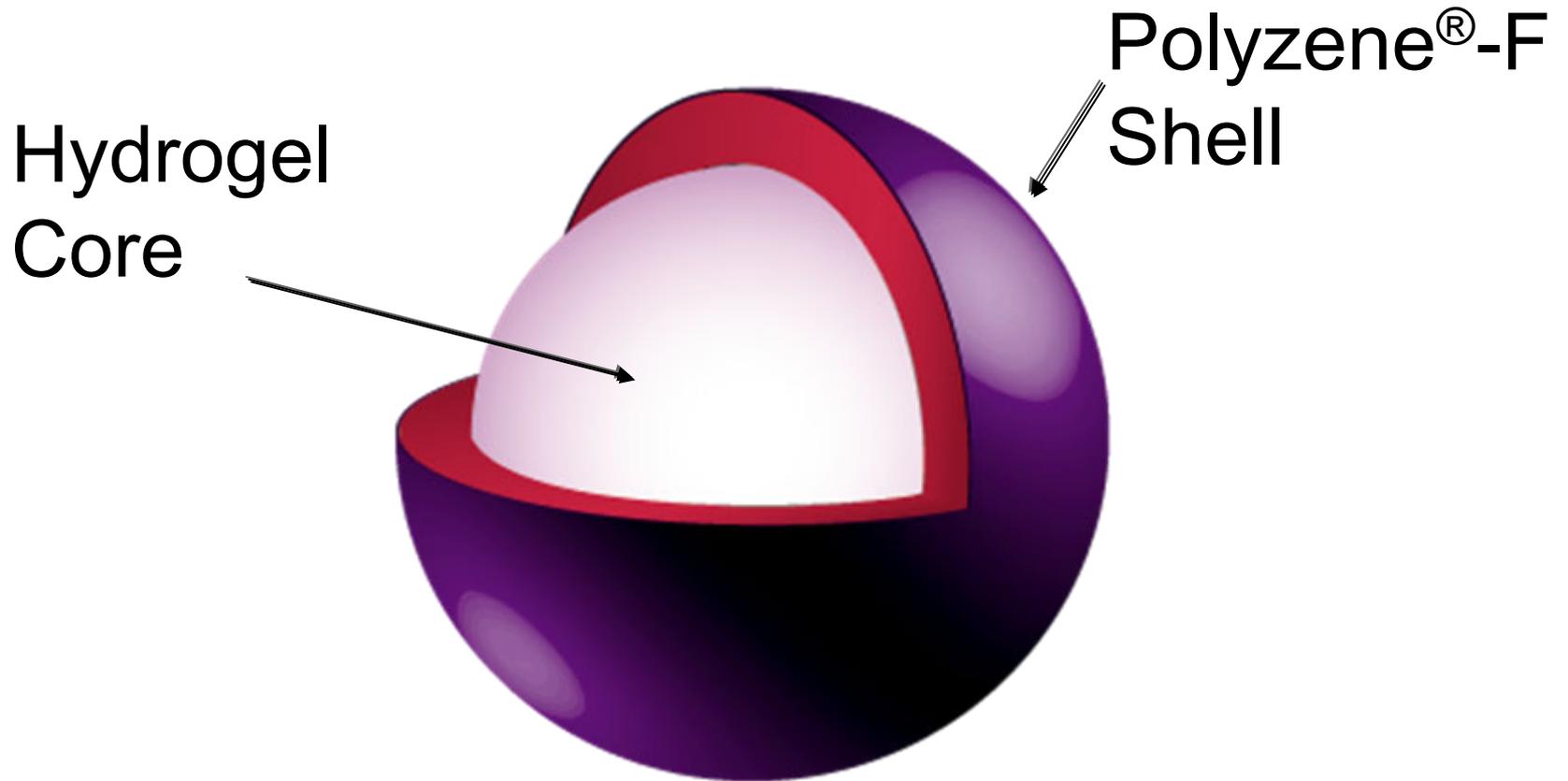


nach DC-BEADS

# .....Neue Embolisate & Liver Tumor

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medikamentenfreisetzende Partikel
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# Embozen® Mikrosphäre

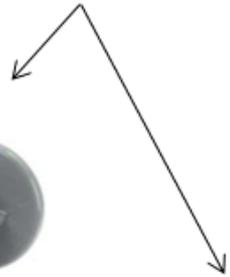


# Embozen® Mikrosphäre

## PVA-Partikel 40-1,300µ

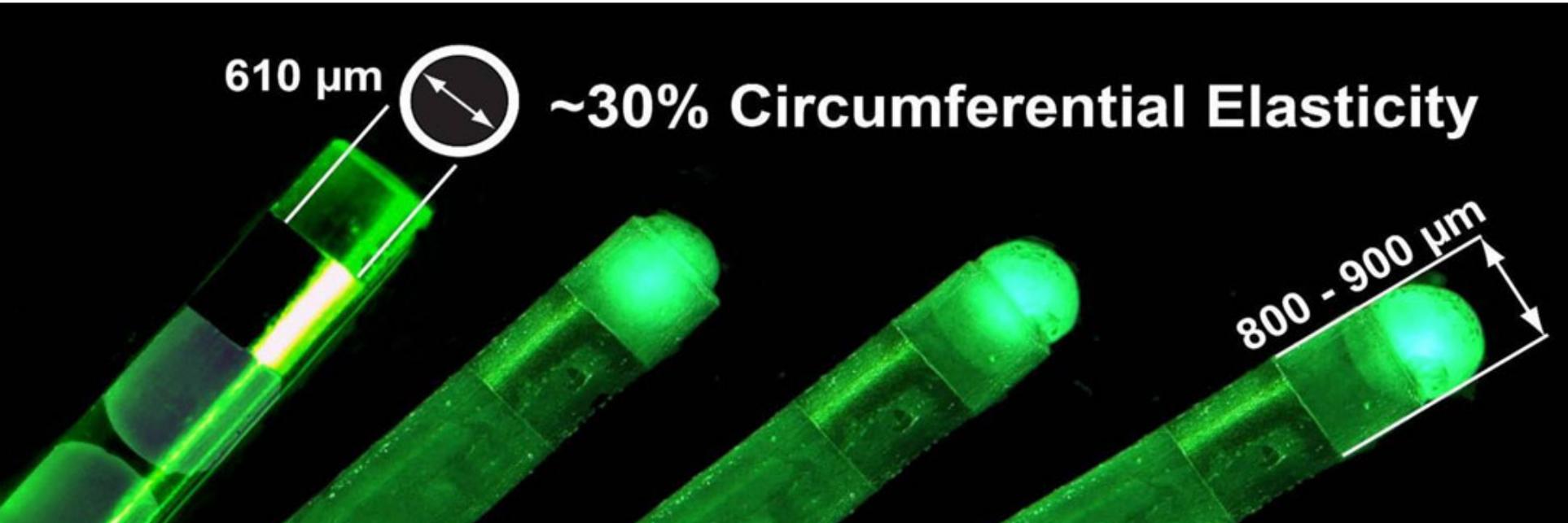
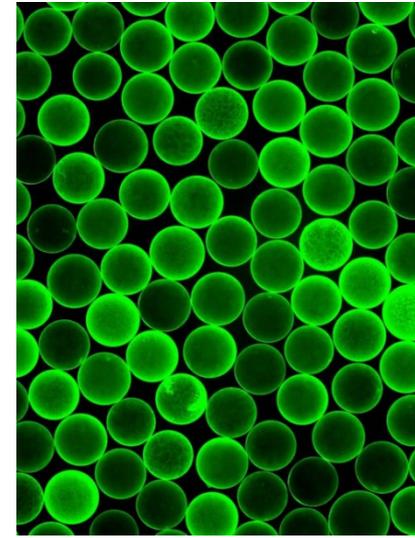


1100 & 1300 µm  
Not Yet Available  
in the US

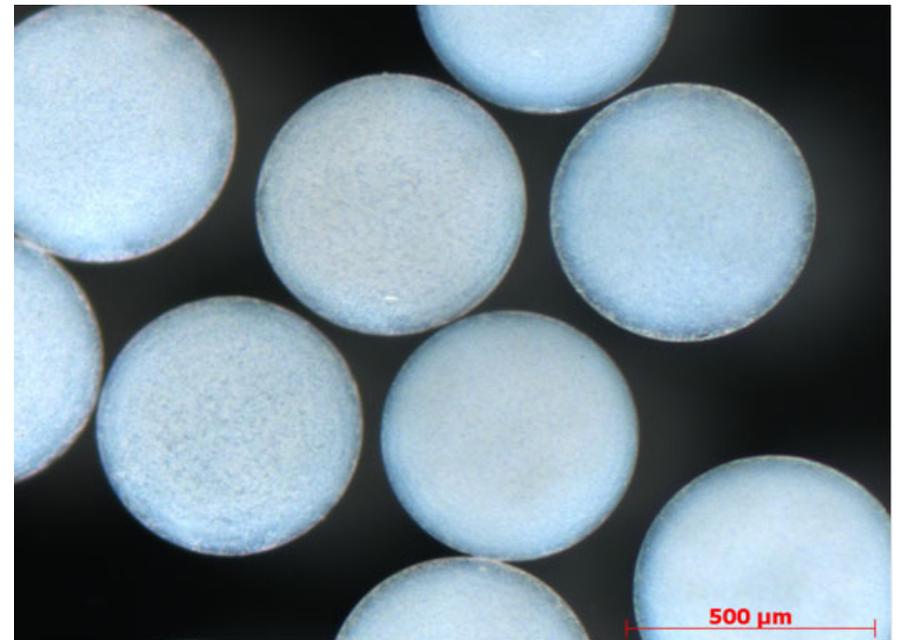
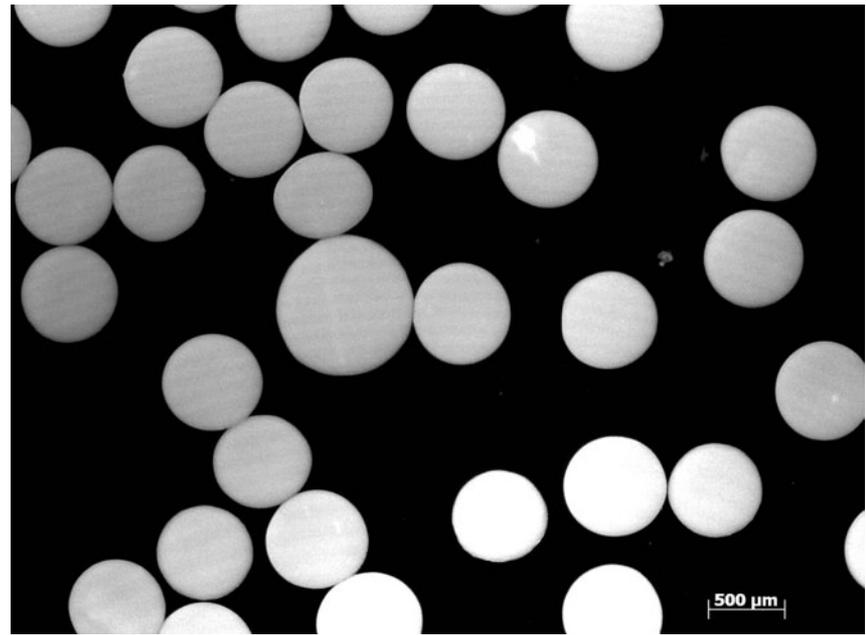
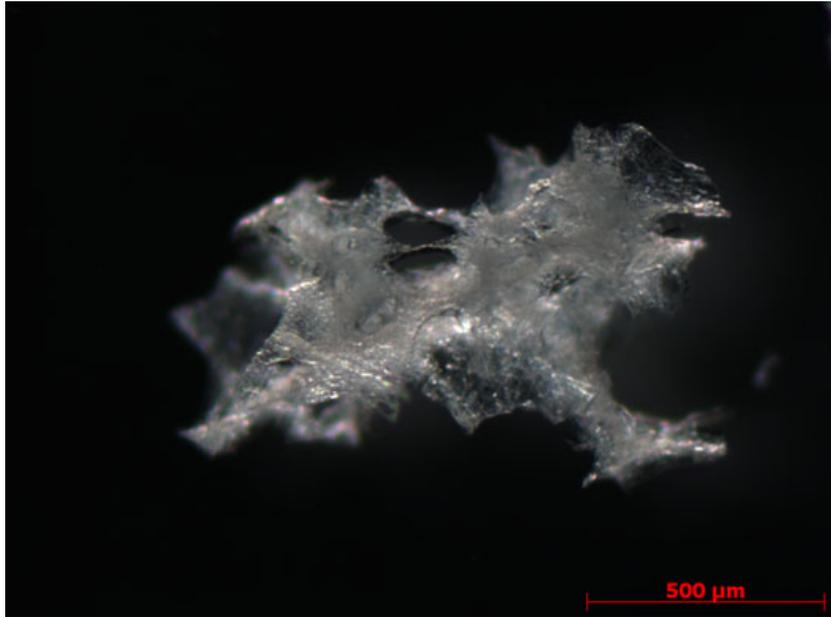


# Embozen® Mikrosphäre

- Genaue Kalibrierung (30% Kompression)
- Biokompatible
- Homogene Suspension, Sphärisch



# Embozen® Mikrosphäre



# Mechanische Stabilität

	Retention of shape	Fragmentierung
Bead Block	96%	5%
Contour	9%	30%
Embosphere	91%	7%
Embozene	95%	1%



The Inaugural Symposium on  
Clinical Interventional Oncology 2009

# Die Rolle der alleinigen Embolization für Lebertumore

- Small vessels need small particles:  
Precise small ( $100\ \mu\text{m}$ ) and very small ( $40\ \mu\text{m}$ ) diameter microspheres
- Avoiding inflammatory reaction ++++  
Truly biocompatible polymer coating

**VEGF-EGFR-Interleukines**

•	$40\ \mu\text{m} \pm 10\ \mu\text{m}$
●	$100\ \mu\text{m} \pm 25\ \mu\text{m}$
●	$250\ \mu\text{m} \pm 50\ \mu\text{m}$
●	$400\ \mu\text{m} \pm 50\ \mu\text{m}$
●	$500\ \mu\text{m} \pm 50\ \mu\text{m}$
●	$700\ \mu\text{m} \pm 50\ \mu\text{m}$
●	$900\ \mu\text{m} \pm 75\ \mu\text{m}$



The Inaugural Symposium on

# Clinical Interventional Oncology 2009

From July 2007

51 pts (HCC&MET)

within approved Institutional Guideline for Clinical Research

N = 25 pts treated for HCC

- 24 pts for evaluation (at least 1 month FU)
- Size: 1.5 up to 12 cm
- 35 selective/super-selective TAE
- 34 target lesions



The Inaugural Symposium on

# Clinical Interventional Oncology 2009

## RECIST CRITERIA

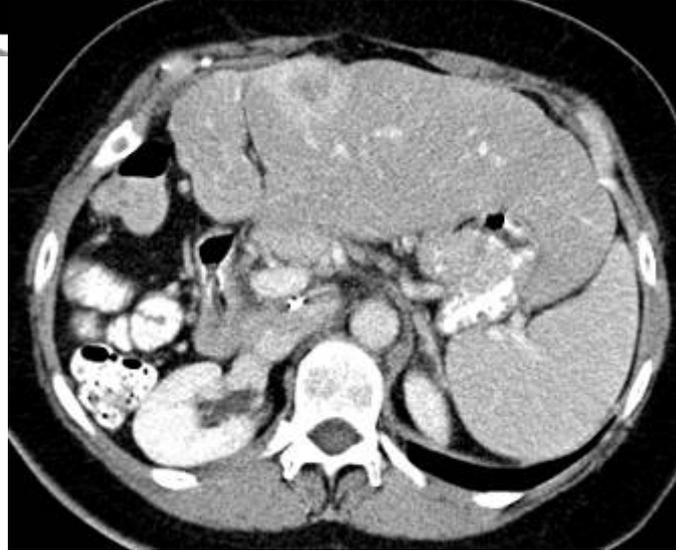
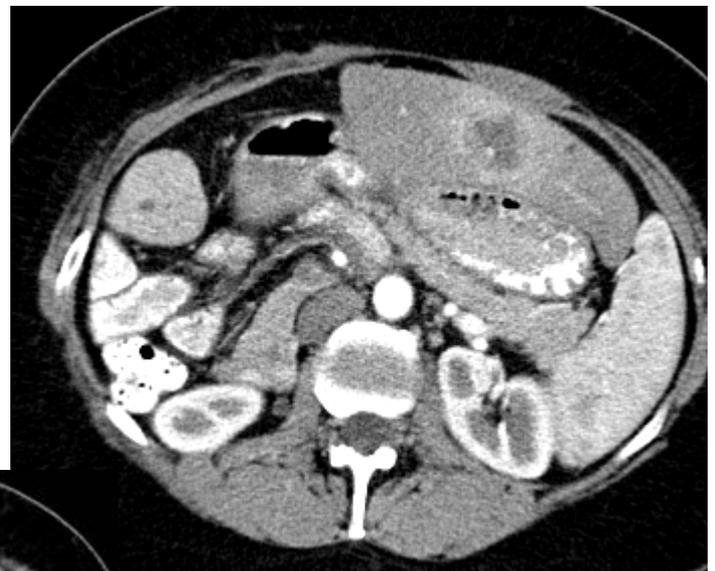
34 HCC nodules

FU (month)	1	3-6	6-12+
lesions	(34)	(25)	(16)
SD	48%	36%	12%
PR	52%	60% (20-73%)	44%
CR			13% (2 lesions disappeared)
PD		4%	31% (available for re-treatment)

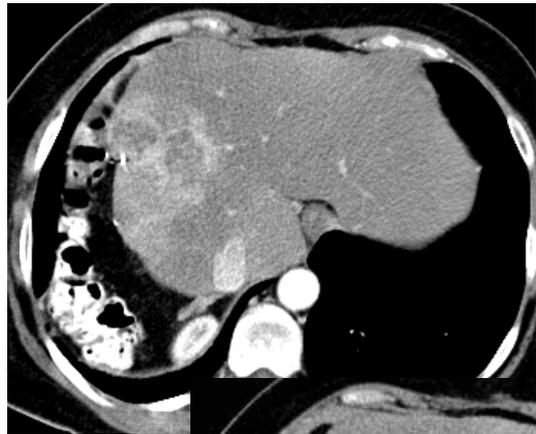
96%

69%

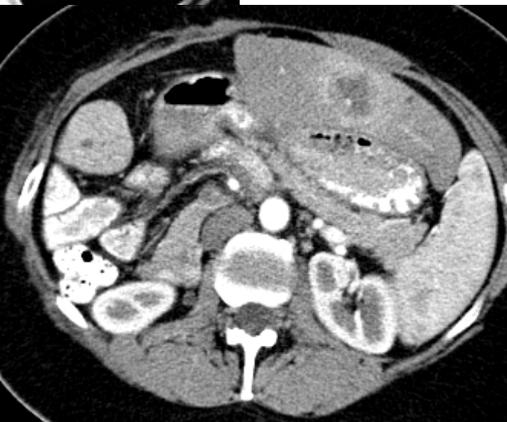
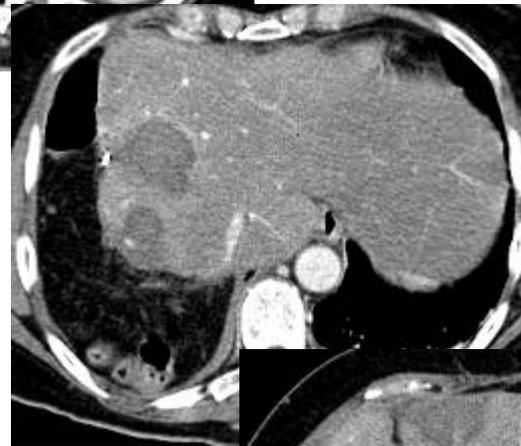
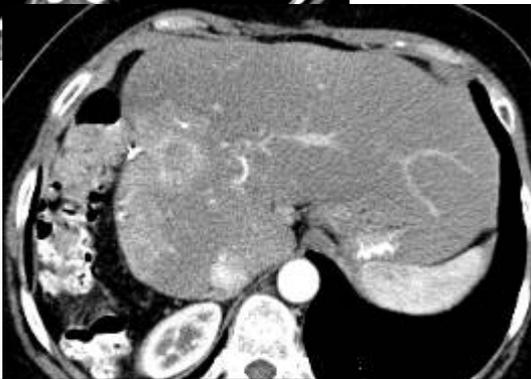
# Embozen® 250 ± 50 µm: bland embolization in CCC



# Embozen® 250 ± 50 μm



4 weeks after  
embolization

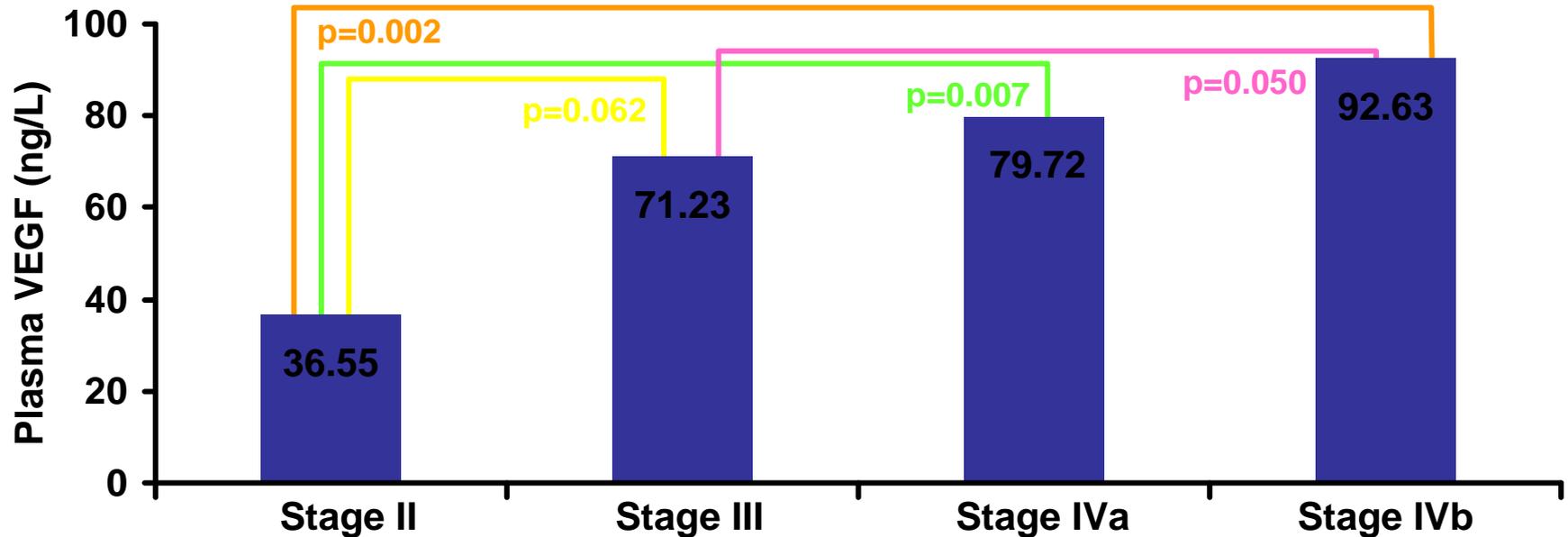


# Negativer Effekt der TACE oder TAE?

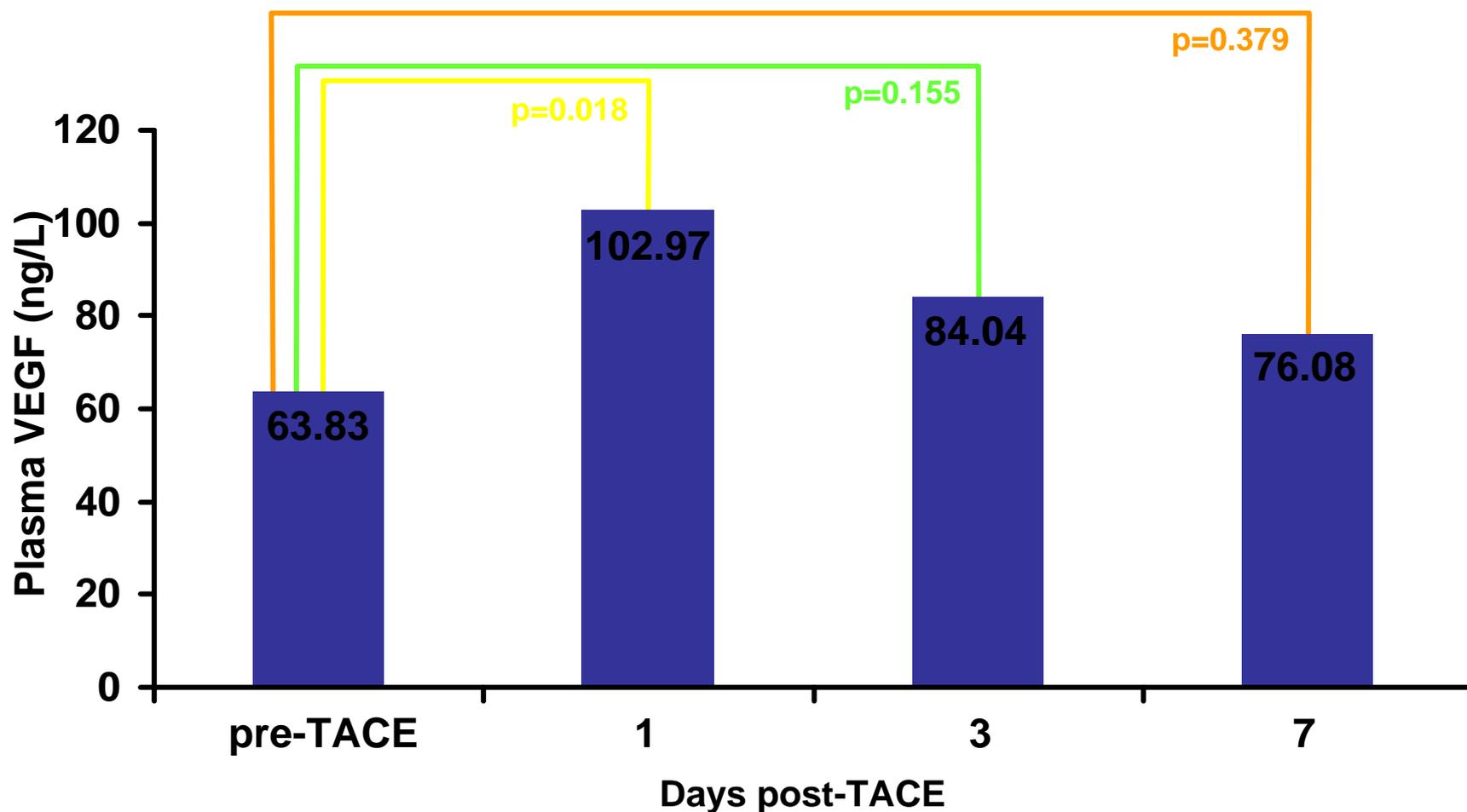
*“Very low inflammatory reaction  
may reduce angiogenesis  
and tumor re-growth”*

# Plasma levels of VEGF in HCC: a key prognostic factor

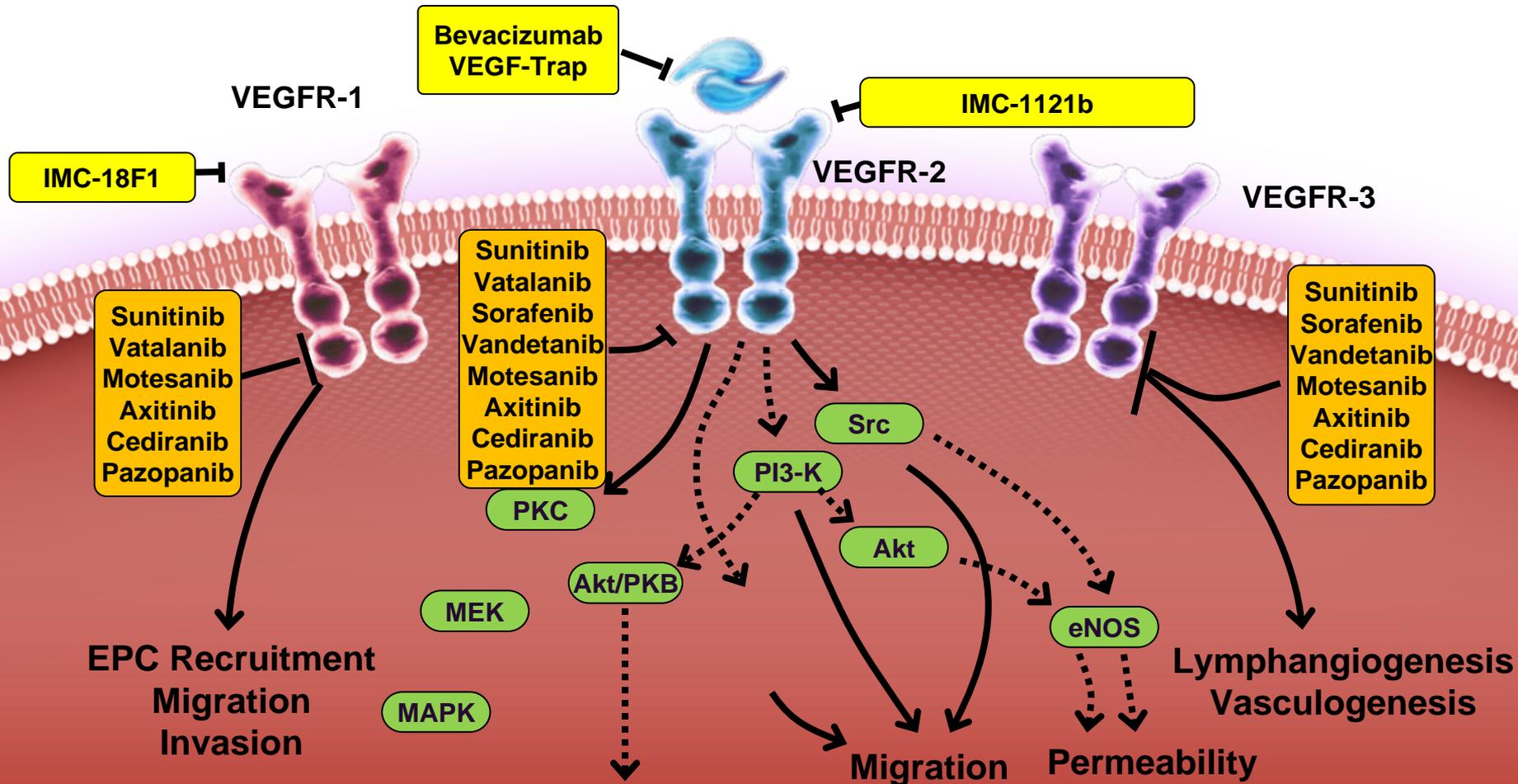
- In HCC, plasma levels of VEGF are increased in patients with:
  - large tumour size ( $p=0.006$ )
  - portal vein thrombosis ( $p=0.011$ )
  - distant metastases ( $p=0.026$ )
  - advanced TNM stage ( $p=0.044$ )



# Plasma VEGF levels significantly increase after TACE through hypoxia

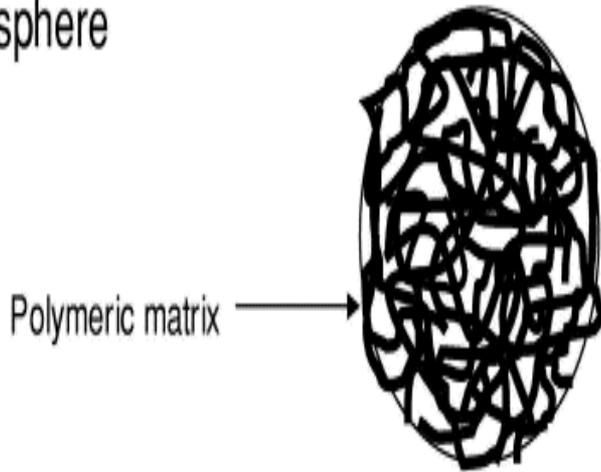


# DEB/Embolization + RFA + anti-angiogenic agents: potential for more synergy?

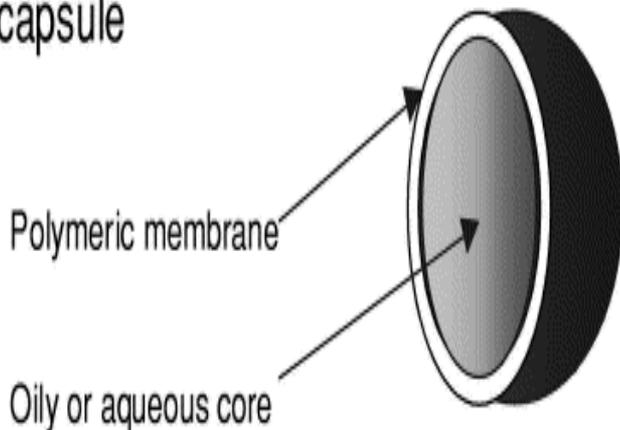


# Polymerische Nanopartikel

Nanosphere

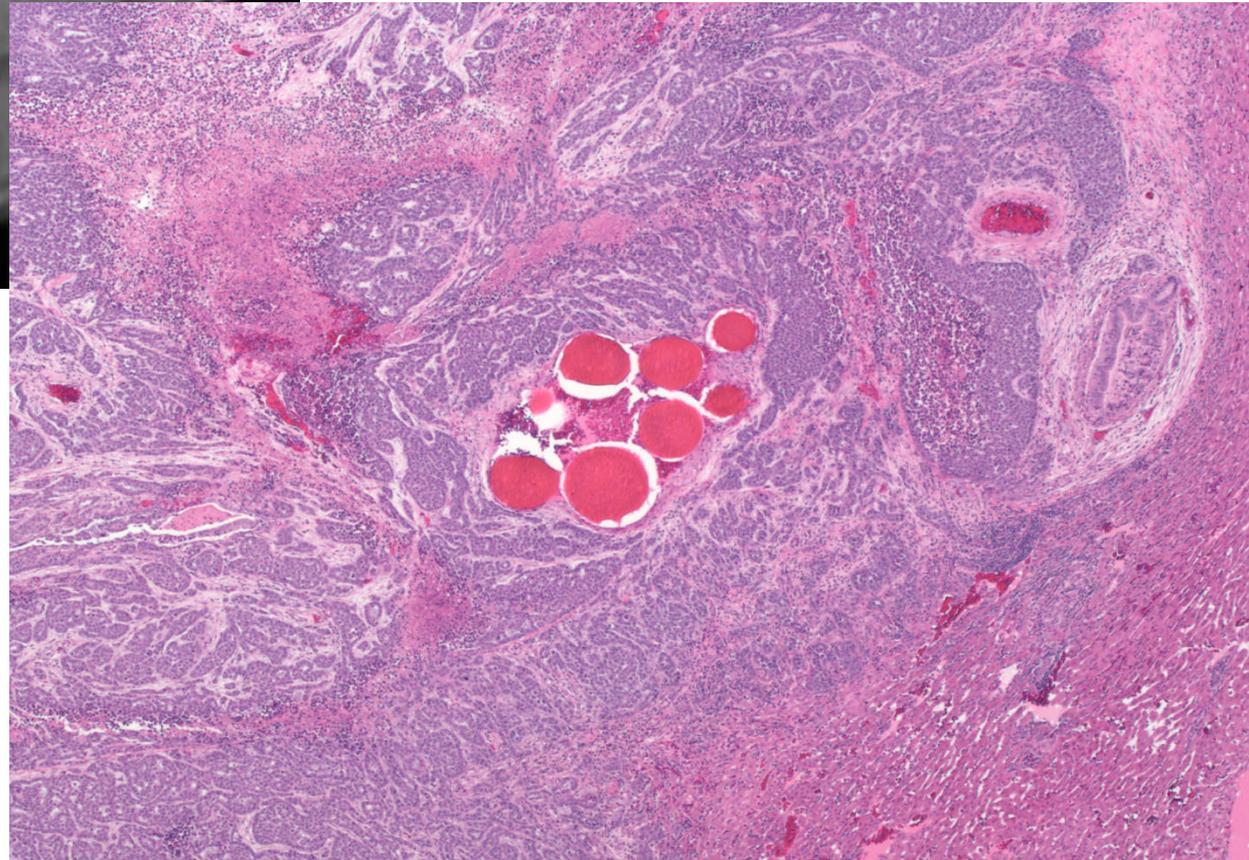
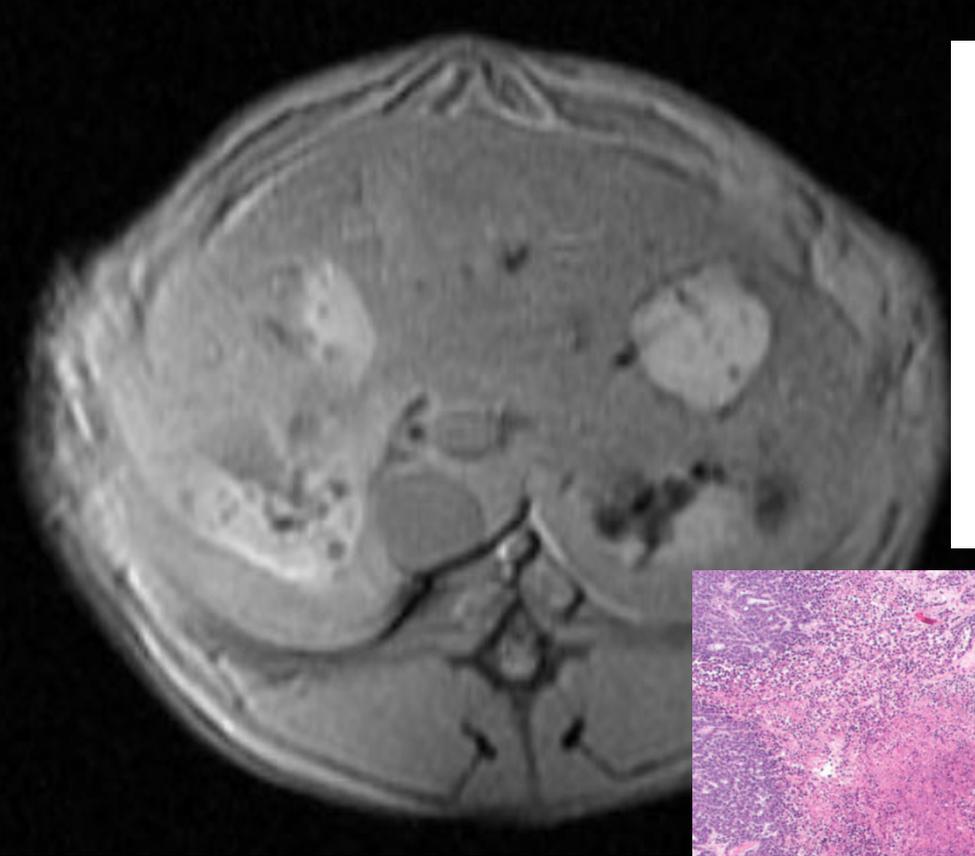


Nanocapsule

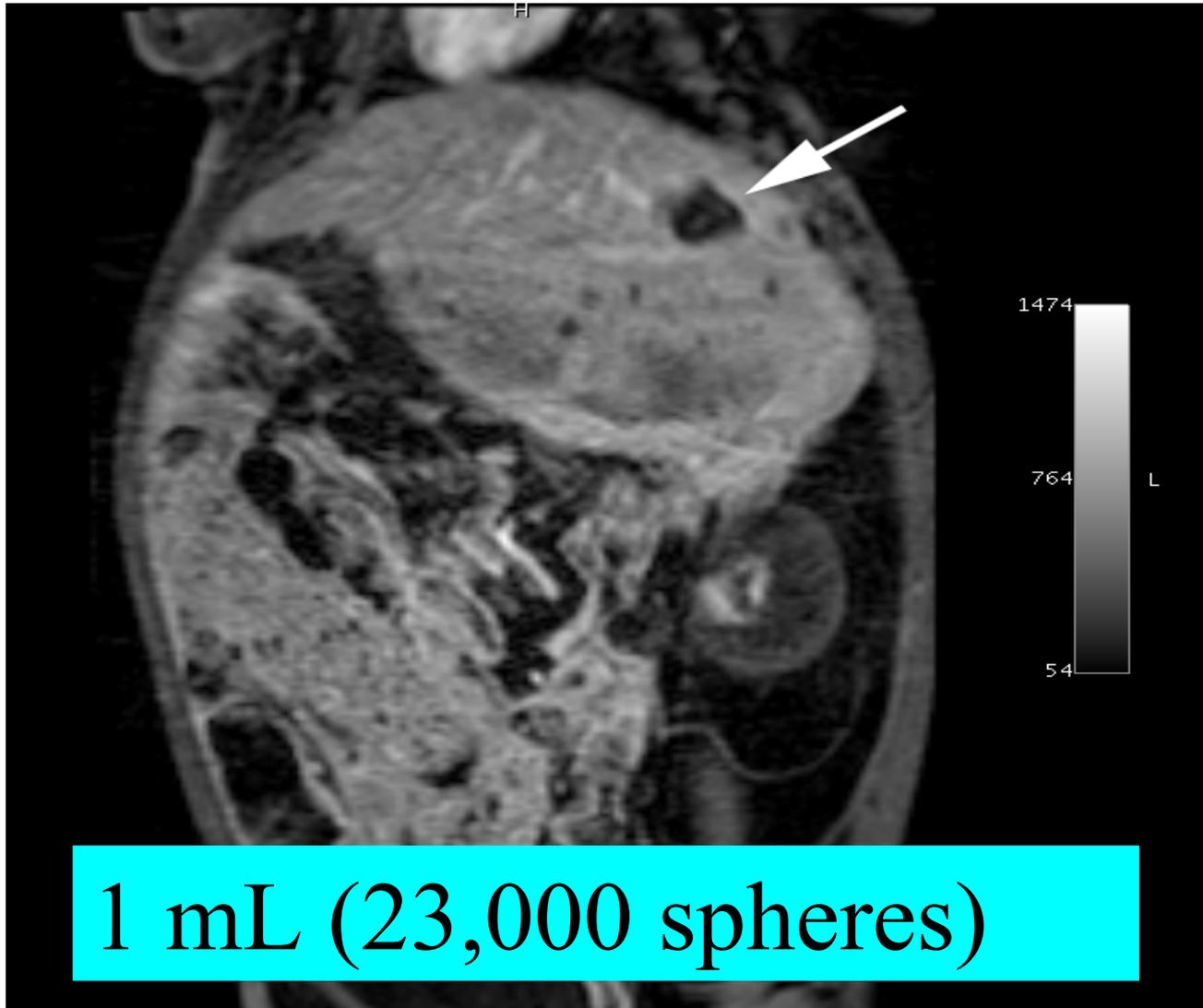


- Small polymeric colloidal particles with a therapeutic agent either uniformly dispersed in polymer matrix (*nanosphere*) or encapsulated in polymer (*nanocapsule*)
- **Examples:**  
Abraxane (ABI-007)  
Magnetic nanoparticles

# IA Therapy for Vx-2 Liver Tumor: Iron-oxide Labeled Nanoparticles



# Rabbit Vx-2 Tumor Embolized with MR-Visible ChemoSpheres



*Courtesy of  
J Geschwind*

# Neue Therapie-Verfahren wie zytostatika-beladene Partikel und blande Embolisation sind vielversprechend....



**Lung Interventions**  
Heilbronn / Germany  
December 11-12, 2009

Local Host  
P. Pereira

Faculty  
T. Grauer  
U. Martens  
P. Pereira  
T. Sobharwal  
T. Vogl

**ESIR** European School of Interventional Radiology

This course is designed for physicians who wish to train their skills in lung interventions. It will impart knowledge of basic and specific therapeutic procedures in order to handle lung biopsies, radiofrequency ablation and chemoembolisation of lung tumours, and bronchial stenting.

Lecturers will focus on latest device technology to obtain successful technical and clinical outcome. Workshops will offer further practical advice complemented by interactive case discussion. The invited speakers are European experts in their field who will also offer web-based support after the course.

Heilbronn is a city in northern Baden-Württemberg, Germany. It is completely surrounded by Heilbronn County and with approximately 120,000 residents it is the sixth-largest city in the state.

The city of Heilbronn is located in the northern corner of the Neckar basin at the bottom of the Wartberg. It is a former imperial free city and a current independent city (i.e. not part of any county) and seat of Heilbronn County.

Viticulture has a long tradition in Heilbronn and is an important part of its economy to this day.

Online registration at [www.cirse.org](http://www.cirse.org)



P. Pereira T. Sobharwal T. Vogl



MÜNCHEN 13.1. - 15.1.2010  
**IROS 2010**  
Interventionell Radiologisches  
Olbert Symposium  
**VORPROGRAMM**

Gemeinsame Jahrestagung der Deutschen, Österreichischen und Schweizerischen Gesellschaft (DeGIR, OGIR & SSCVIR) für Interventionelle Radiologie

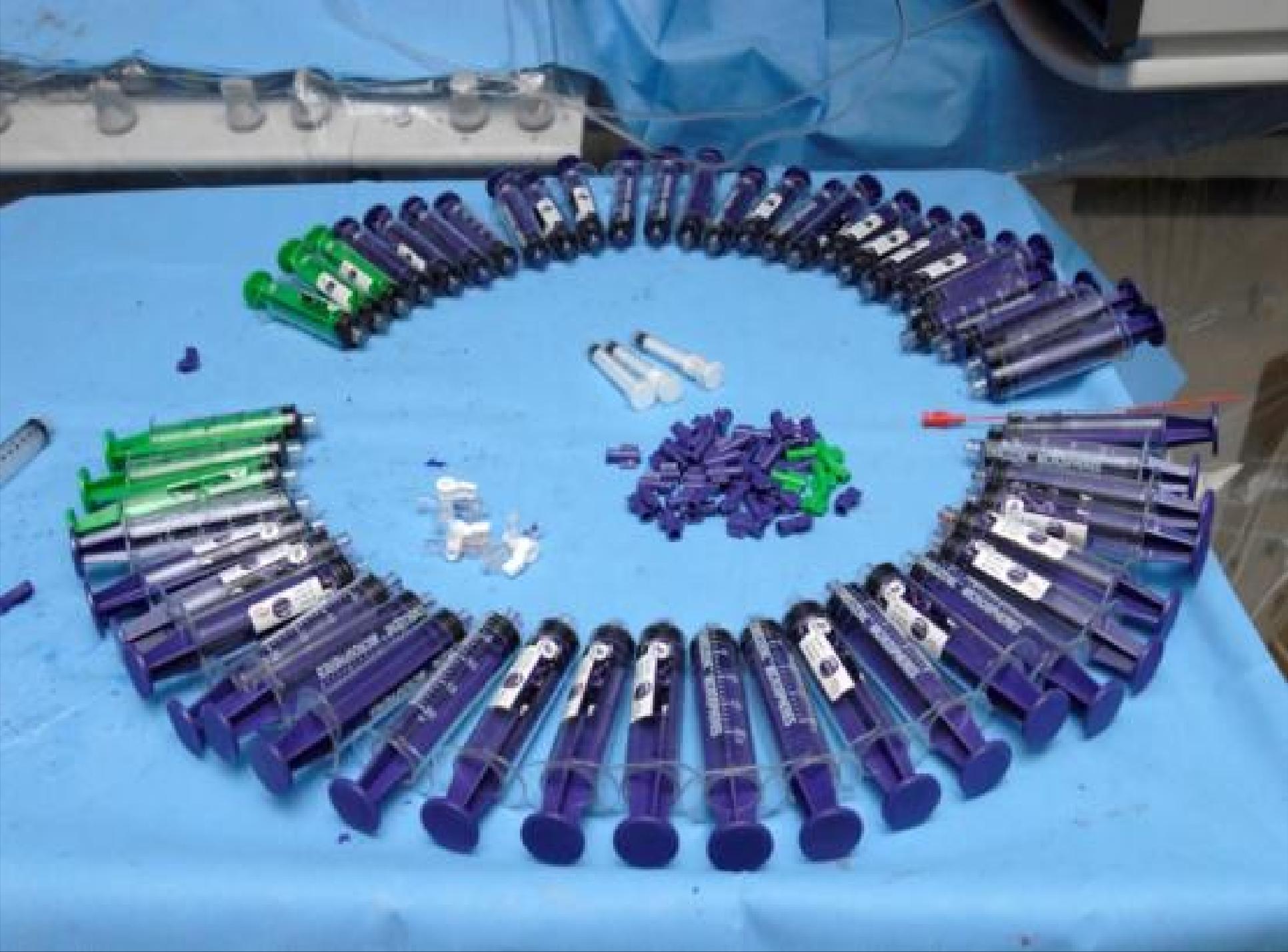


**4TH ESGAR**  
**IMAGE-GUIDED ABLATION**  
**WORKSHOP (IGA)**

Munich, Germany  
February 22 - 23  
2010



# Danke !



# Recommendations for further studies

1. Embolization results in **hypoxia** that may lead to neoangiogenesis through production of **VEGF**
2. **New embolization combined with RFA** has now to be prospectively studied
3. ....there is evidence to support the investigations of **embolization ± RFA in combination with new anti-angiogenic agents**



New embolization + RFA ± Antiangiogenic ?