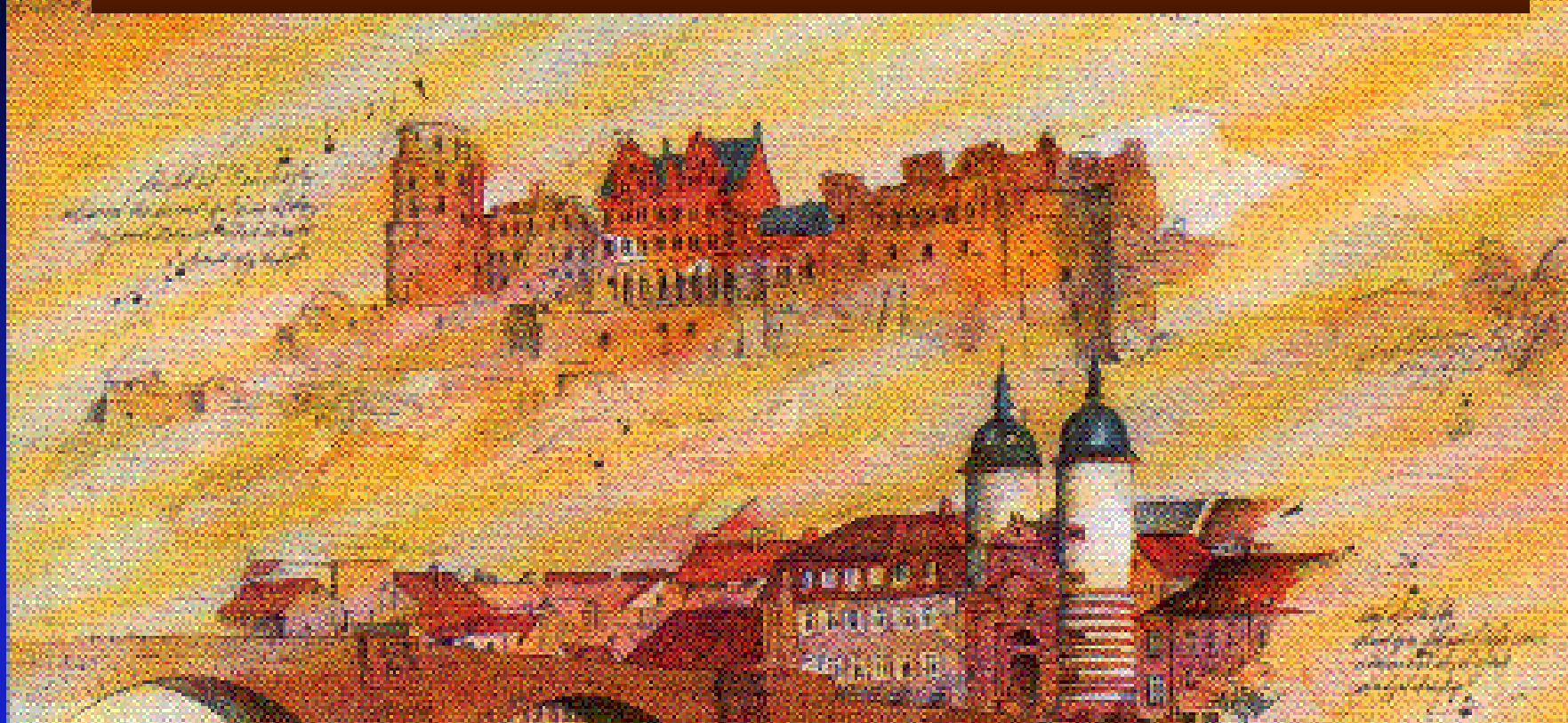


Future Directions of Embolotherapy: Materials, Designs and Combined Treatment Concepts

G.M. Richter, University Hospital, Heidelberg



Disclosures: Consultant, Grant Recipient, CeloNova BioSciences

Clinical Background

Benign Tumors: UFE

Malignant Tumors: HCC, RCC

Vascular Disease: Endoleaks, AVM

UFE: Requirements and Expectations

Technical success

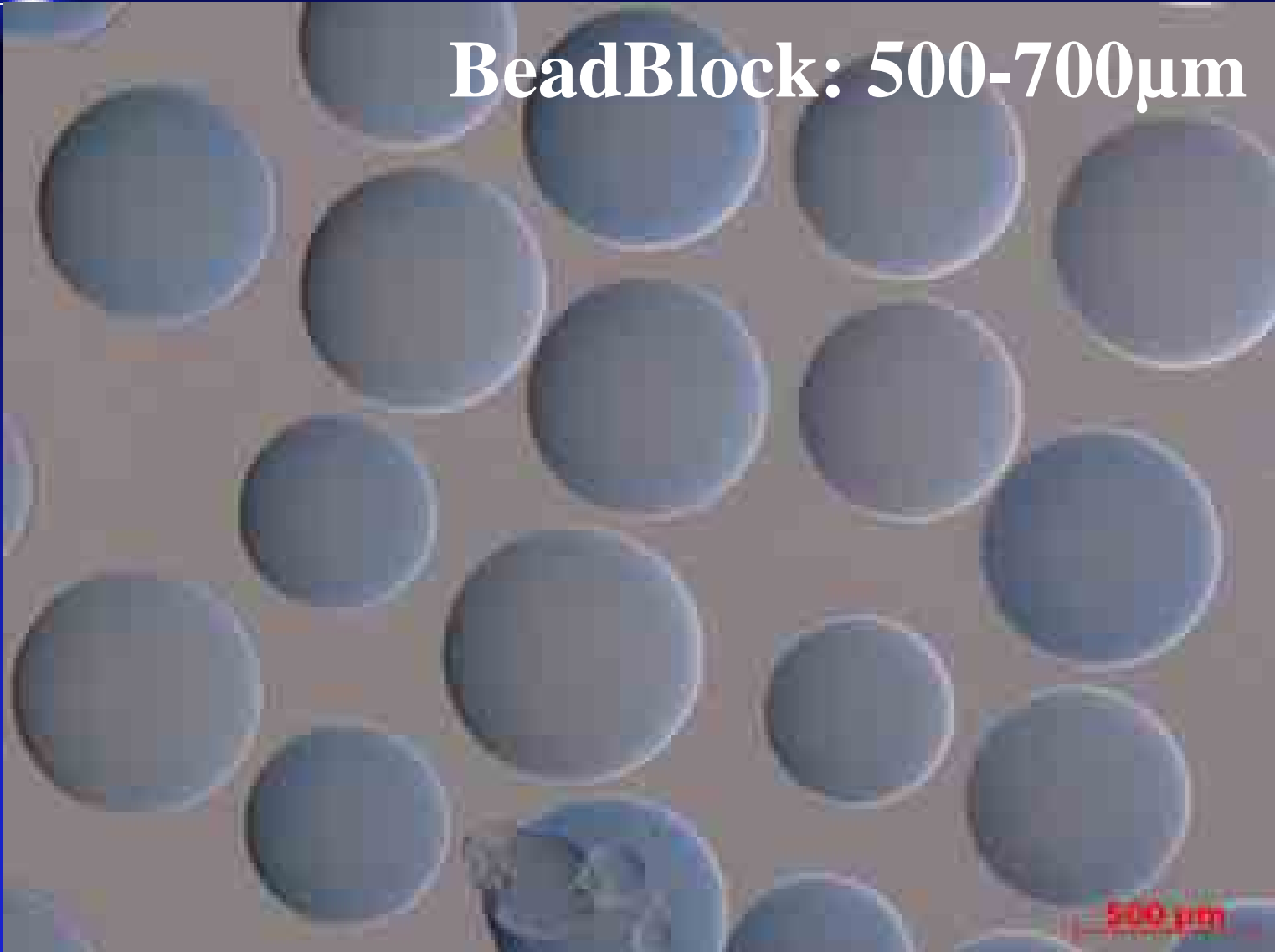
handling, mechanical behaviour

Clinical success

devascularization, biocompatibility

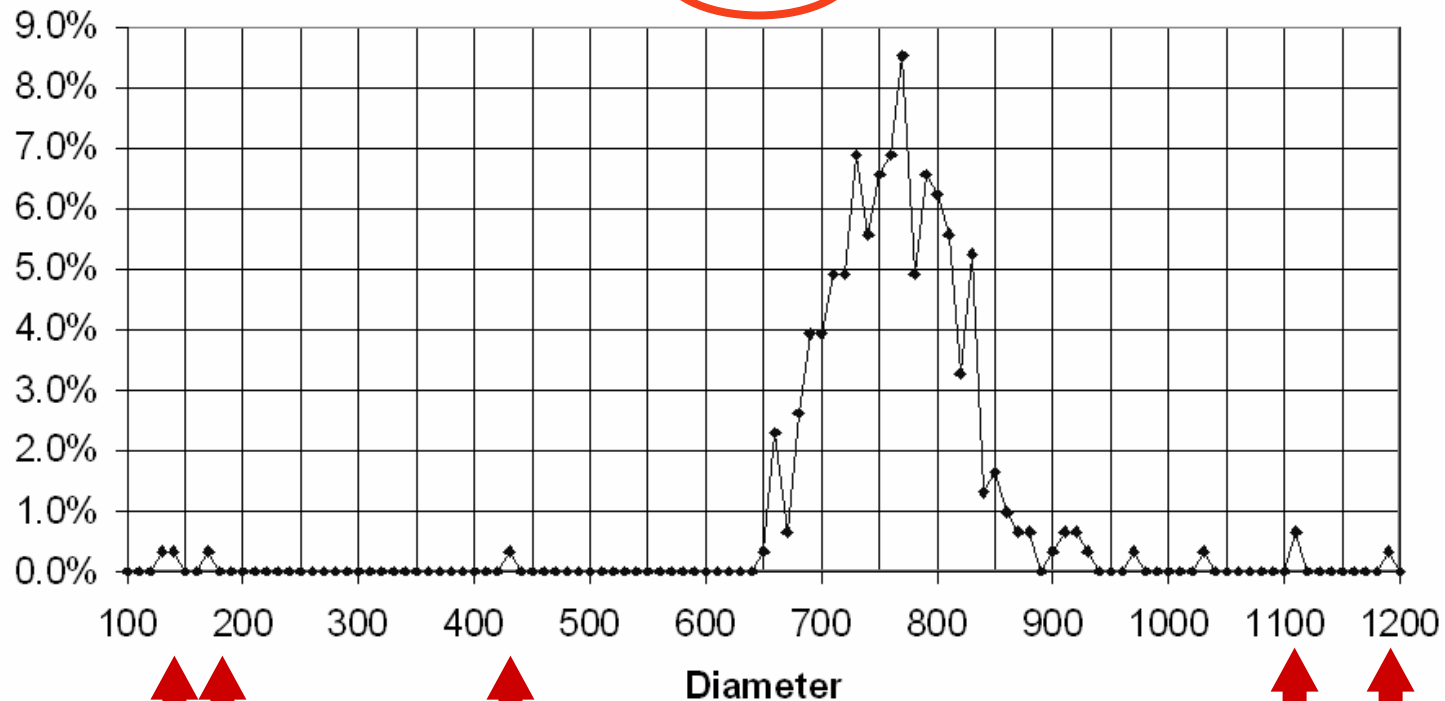
Significance of Calibration Precision

BeadBlock: 500-700 μ m

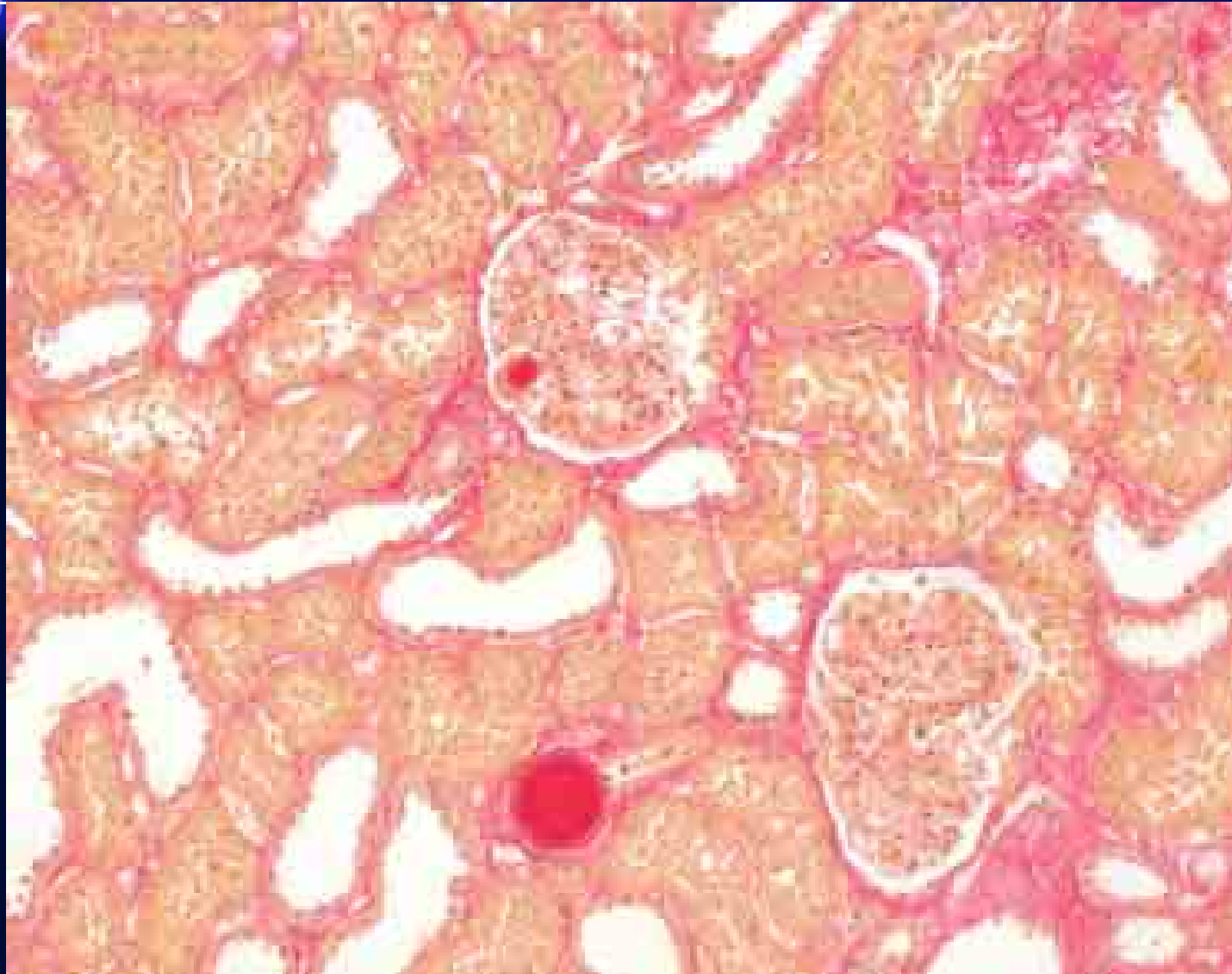


Significance of Calibration Precision

700 - 900 μm Embosphere in 50% Imeron 300
Date of Measurement: September 9, 2005; Median: 758,5 μm
Target Bandwidth [μm]: 300; Oversized particles: 3,28%; Undersized particles: 15,08%



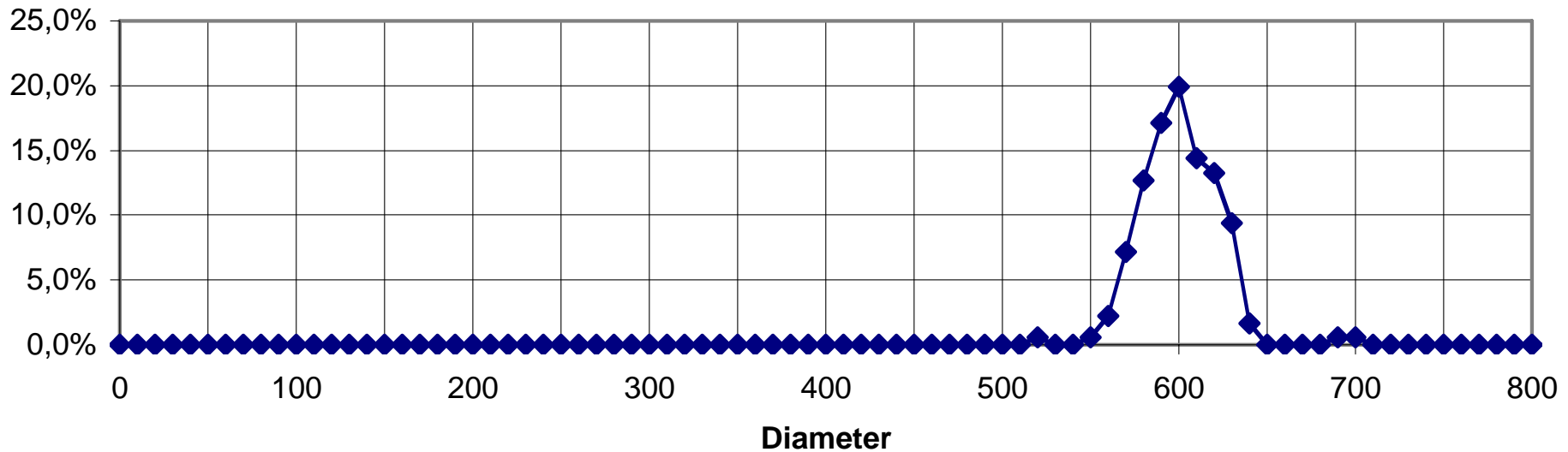
Why is Calibration Precision Important?



Embozene

Enhanced Precision by Enhanced Calibration

500 μm class
Date of Measurement: August 28, 2005; Median: 595 μm
Target Bandwidth [μm]: 100; Oversized particles: 1,1%; Undersized particles: 0,55%

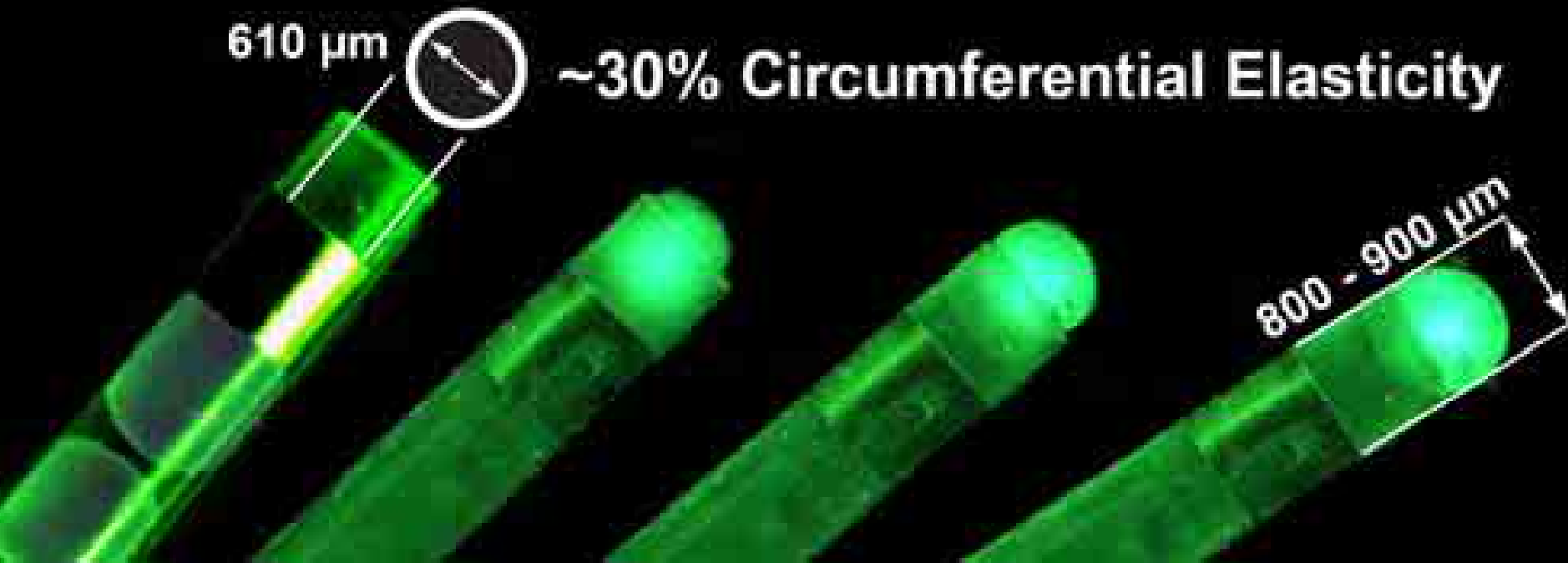


Determination of Mechanical Stability



Determination of Mechanical Stability

700- 900 μm , 610 μm Catheter

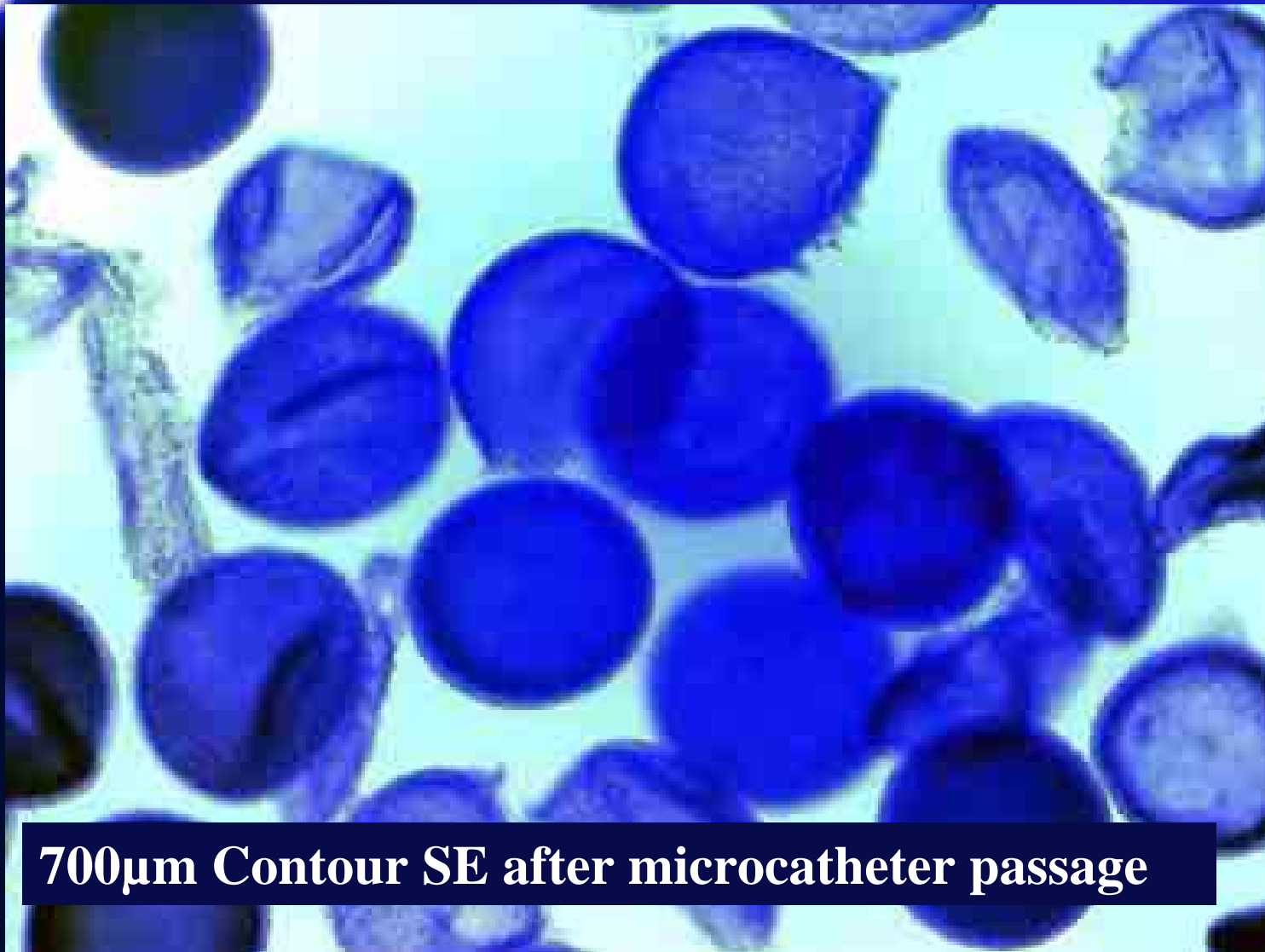


Embosphere



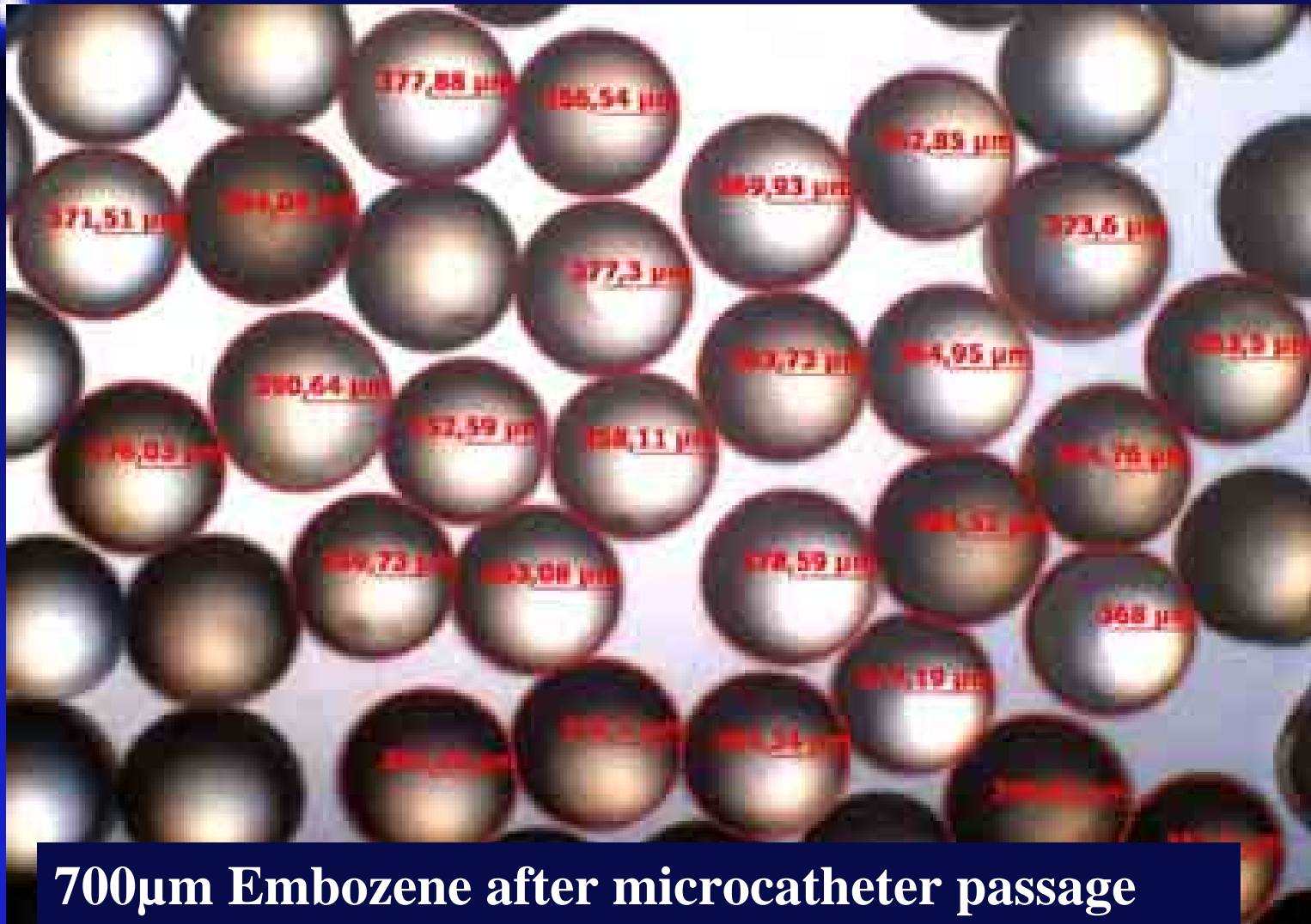
700 μ m Embospheres after microcatheter passage

Contour SE



700µm Contour SE after microcatheter passage

Embozene

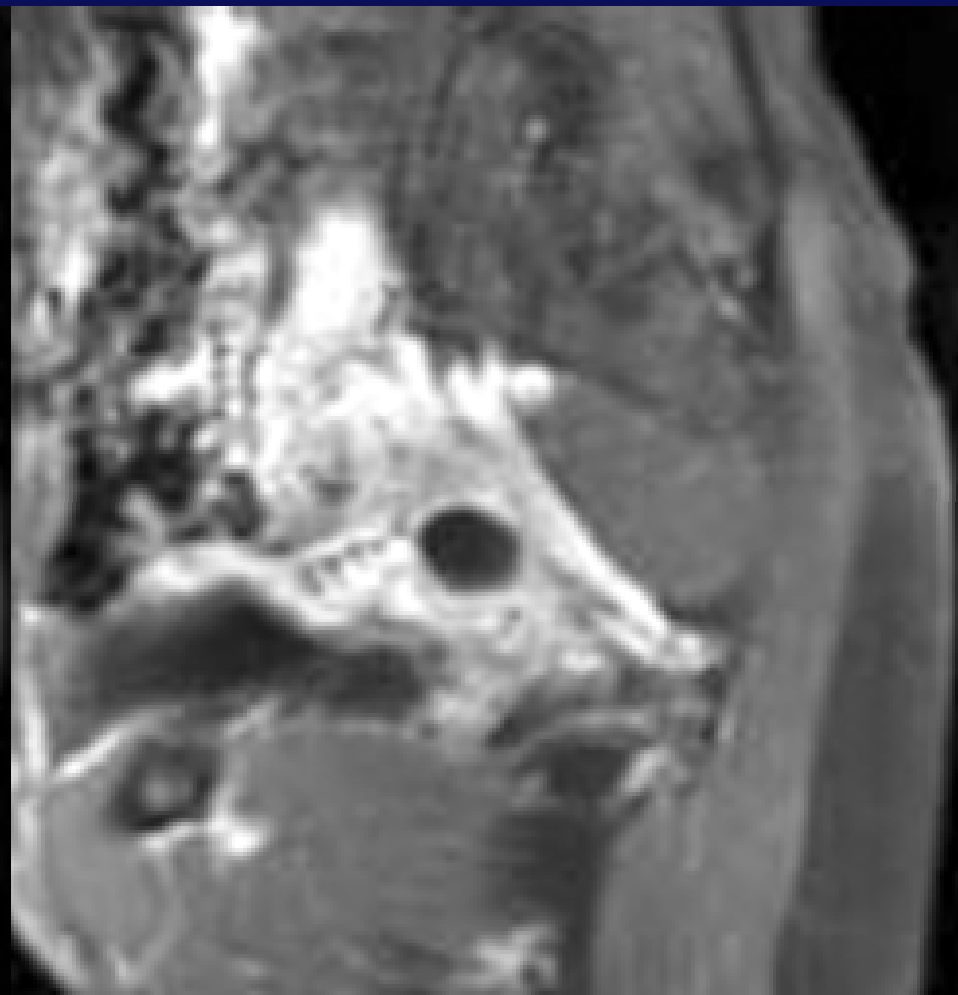
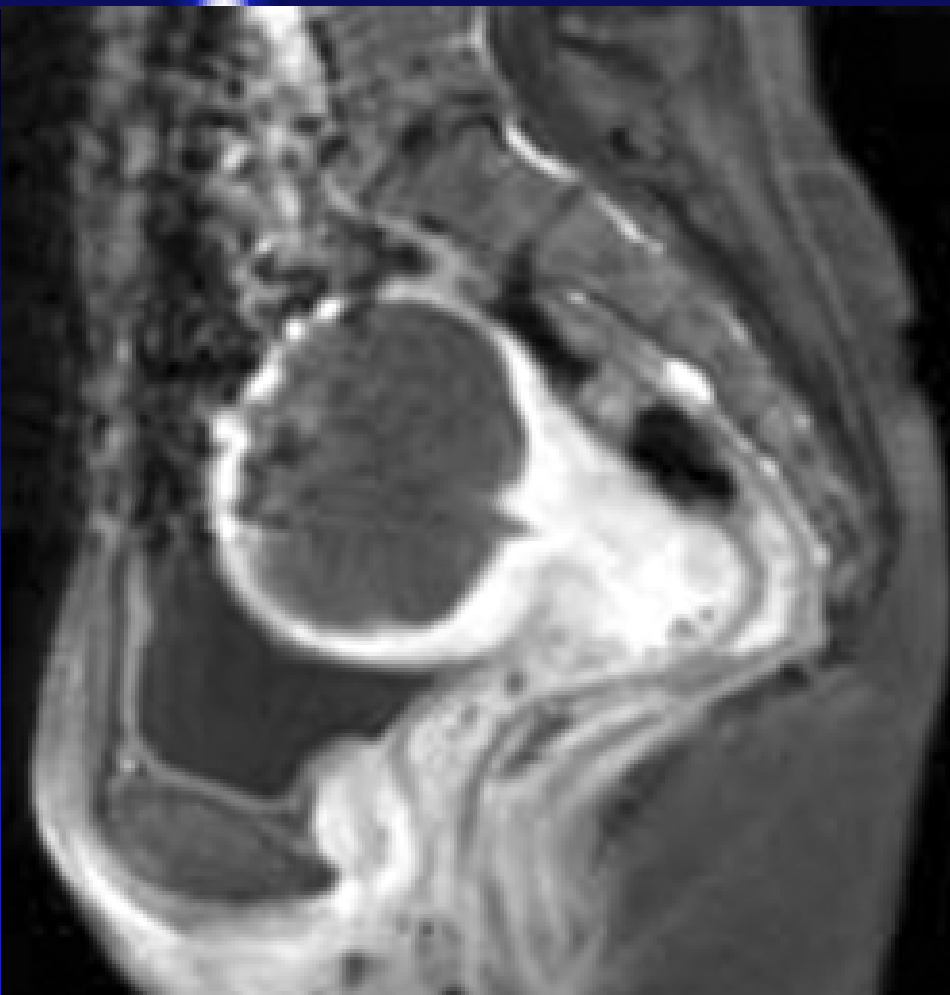


Results:

700- 900 μm , 610 μm Catheter

	Retention of Spherical Shape	Fragmentation
Bead Block	96%	5%
Contour	9%	30%
Embosphere	91%	7%
Embozene	95%	1%

Clinical Success: Devascularization + Biocompatibility



Recognition as „Foreign“

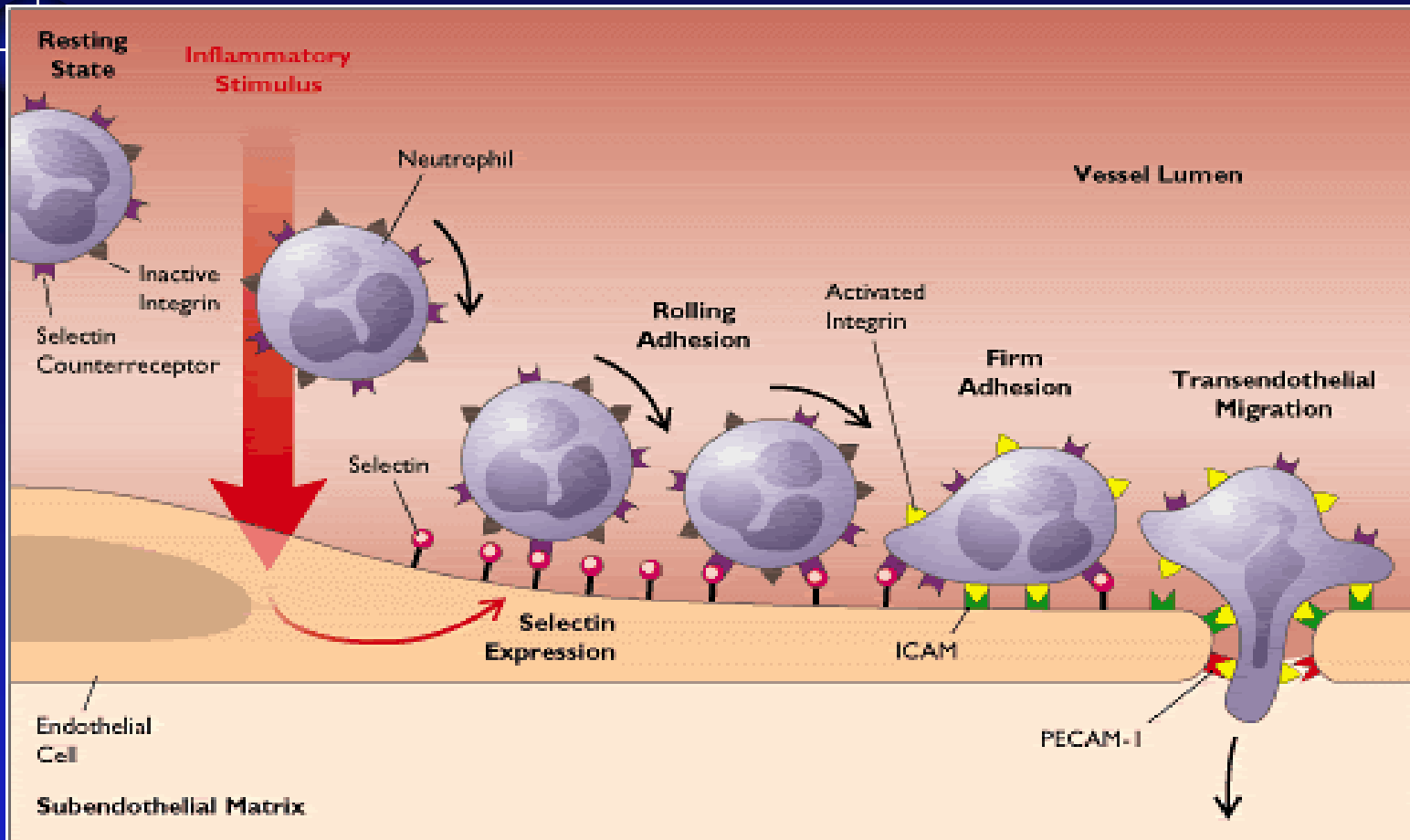


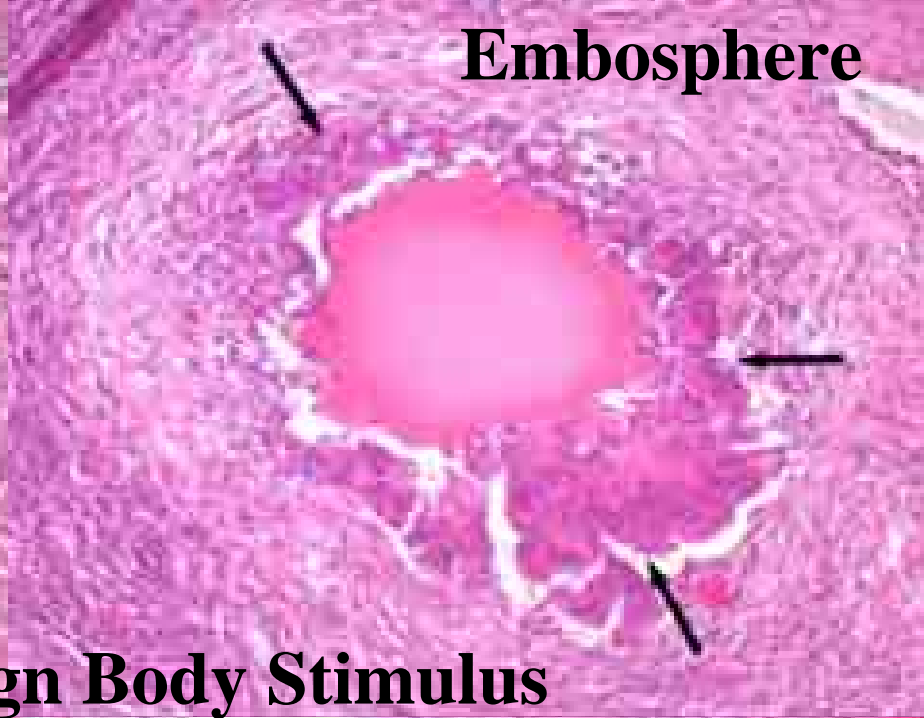
Figure 1. Cell-to-cell adhesions that enable a neutrophil to leave the circulation begin with both the neutrophil and the vascular endothelium in a resting, noninteractive state. Activated by an inflammatory stimulus, the endothelium expresses selectins, whose binding to their receptors on neutrophils initiates a rolling adhesion of neutrophils

to the vessel's luminal wall. The neutrophils activate their integrins, which bind to endothelial ICAMs, permitting a firmer, stationary adhesion. Transendothelial migration may be guided by further adhesive interactions, perhaps involving molecules such as PECAM-1, which endothelial cells express at intercellular junctions.

Embozene

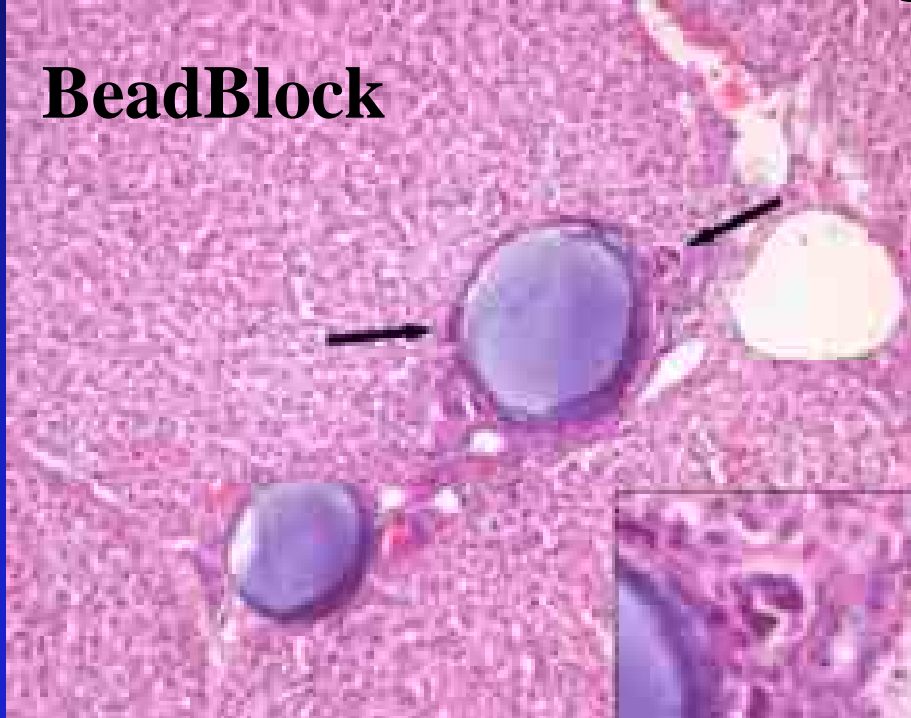


Embosphere

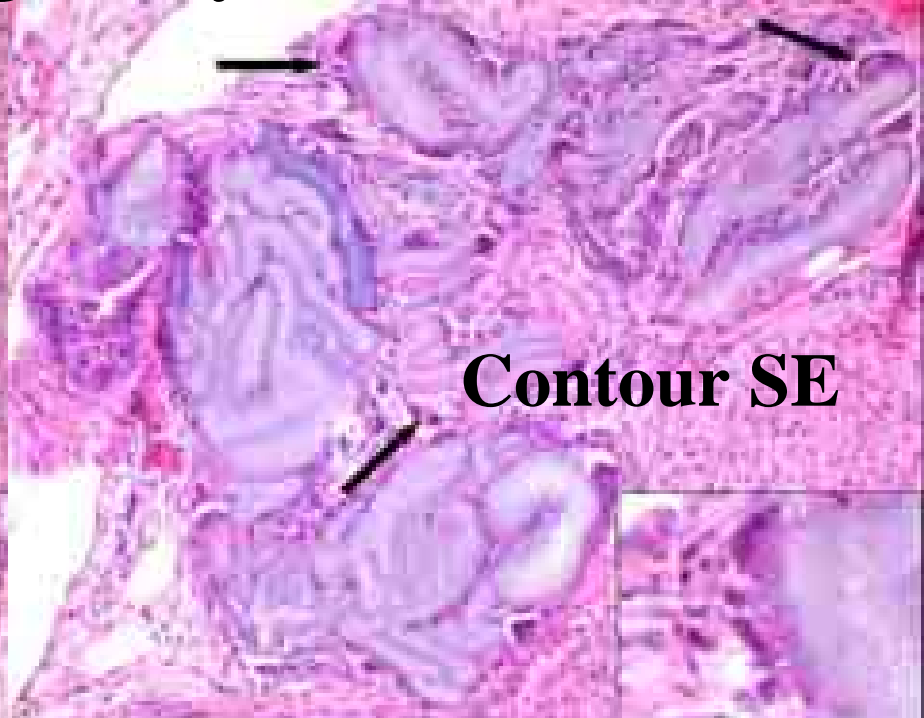


Giant Cell = Foreign Body Stimulus

BeadBlock



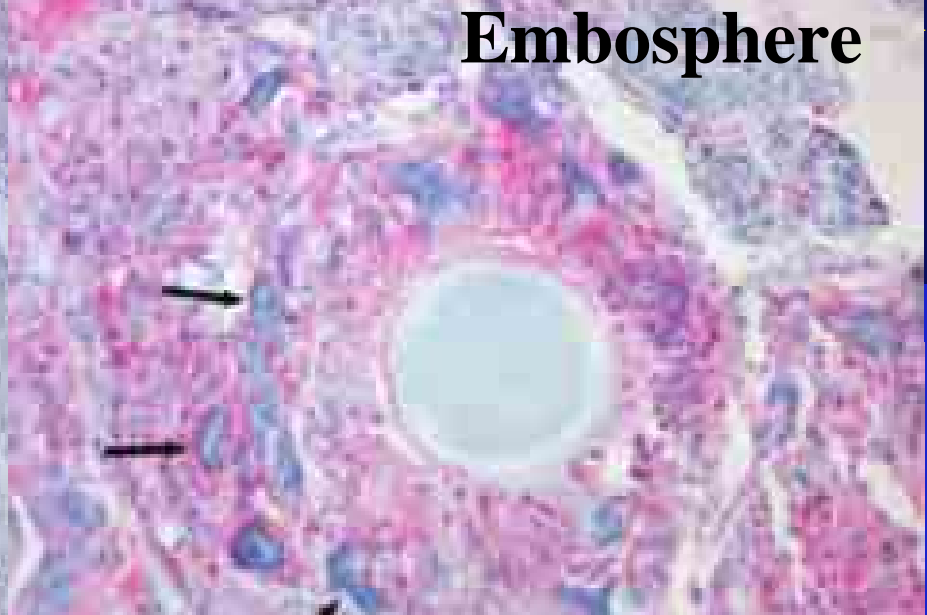
Contour SE



Embozene

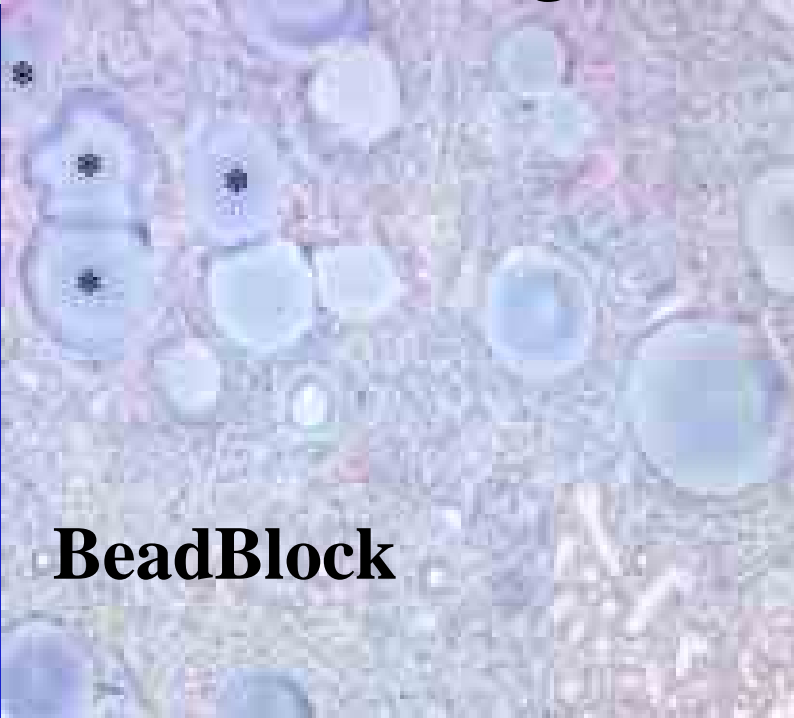


Embosphere



CRP immunostaining = non-anoxia related inflammation

BeadBlock



Contour SE



Clinical Background

Benign Tumors: UFE

Malignant Tumors: HCC, RCC

Vascular Disease: Endoleaks, Aneurysms

HCC: Requirements and Expectations

Technical success

vascular anatomy, concept selection

Clinical success

devascularization, durability

Multiplicity of Options

Sphere only (bland embolization)

Lipiodol + drug (conventional TACE)

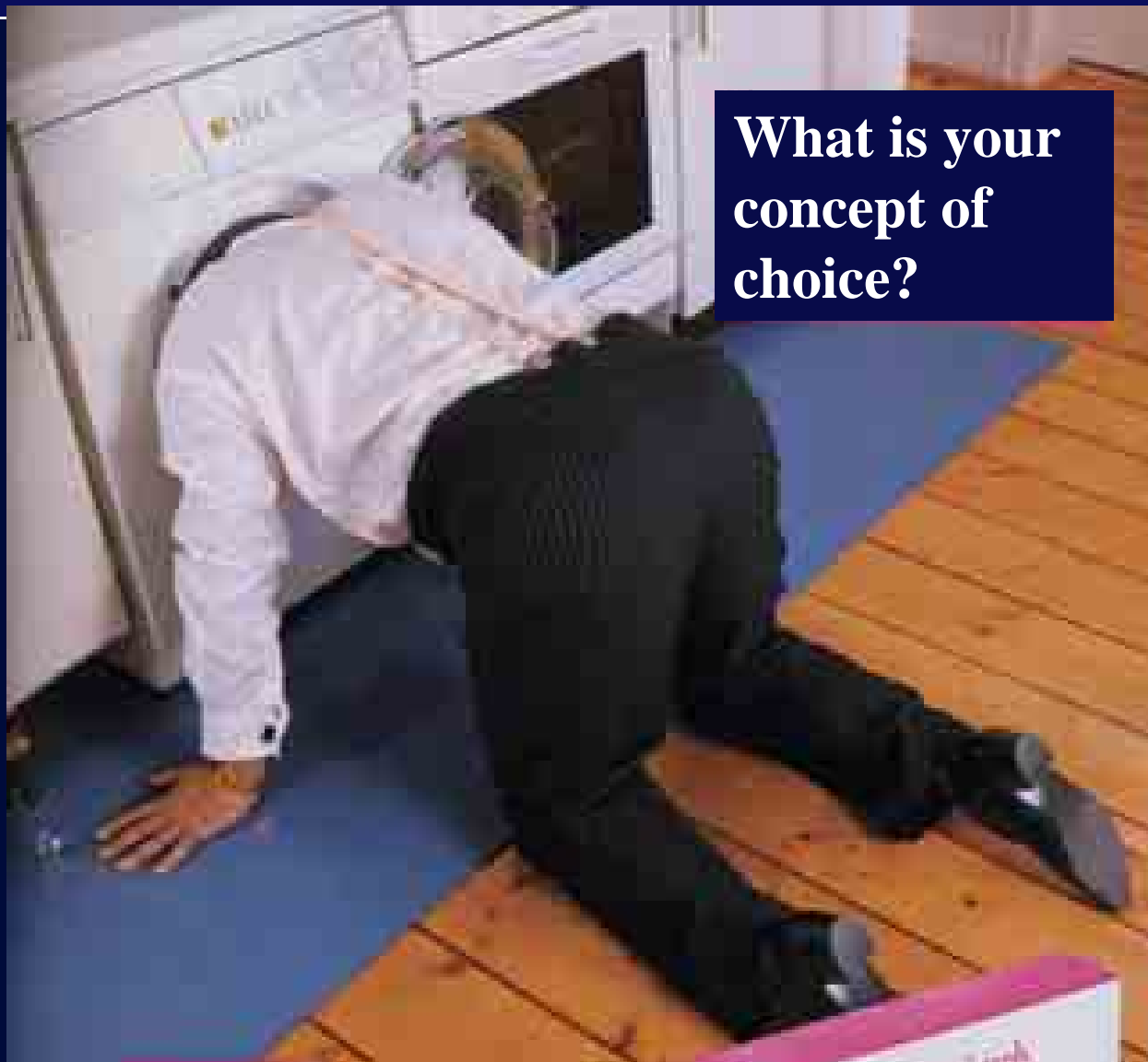
Lipiodol + drug + sphere (small - medium - large)

Expanding sphere (Hepasphere Concept)

Drug delivering sphere (Precision TACE Concept)

Interstitial irradiation sphere (Sirtex Concept)

Multiplicity of Options



What is your
concept of
choice?

HCC and Cytostatic Drugs

John Terblanche:

..no single drug, or combination of drugs, has a consistent response rate of more than 20%

Drugs for TACE:

Cytostatic efficacy independant from cell cycle

Passive membrane transport

Highest local concentration

Increased efficacy by factor 3

HCC and Anoxia

HCC in cell culture:

4h anoxia **minimal growth reduction**

8h anoxia **doubling 2-3 fold prolonged**

12h anoxia **growth stopped for days**

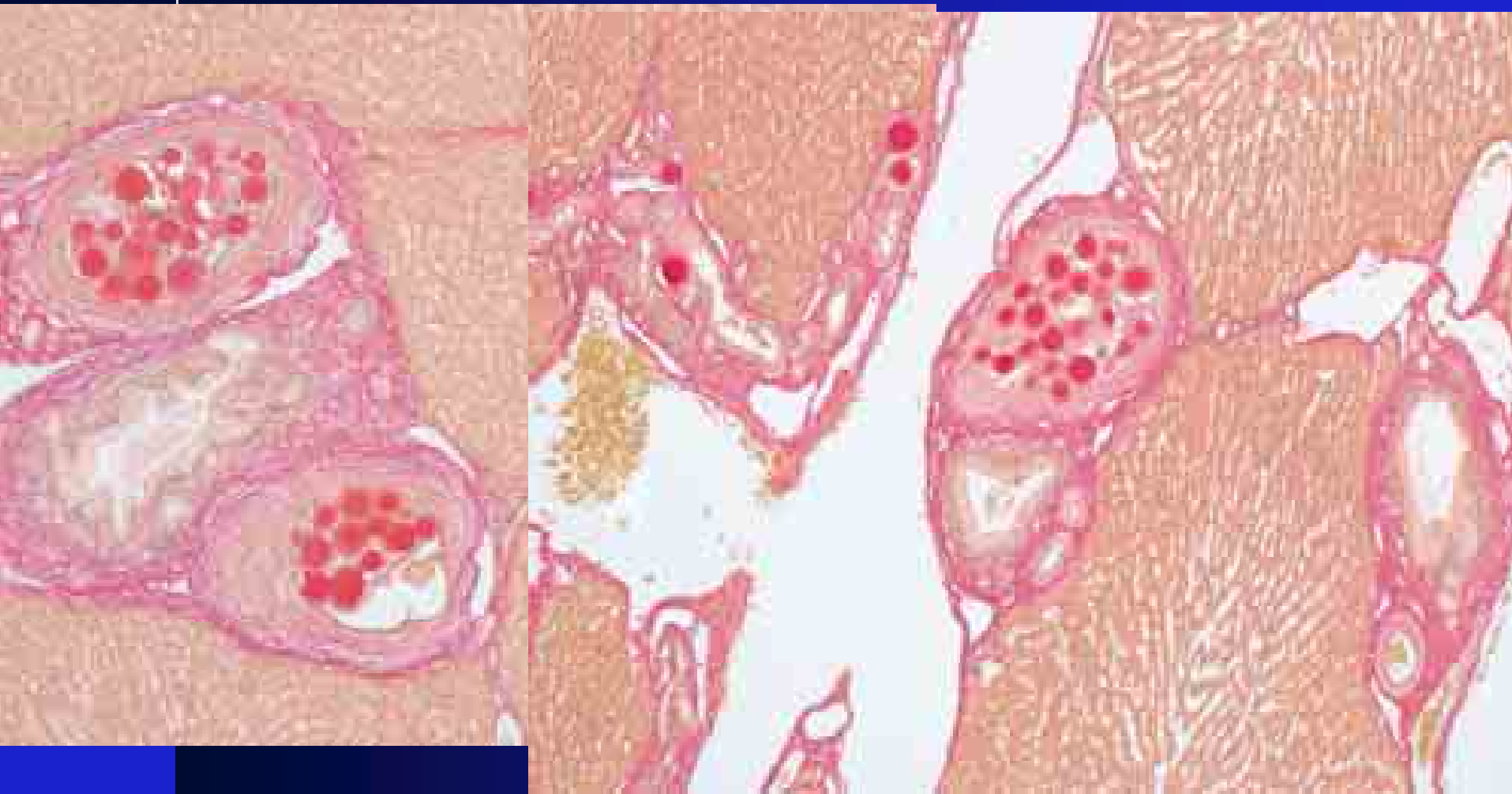
> 24h anoxia **100% cell death**

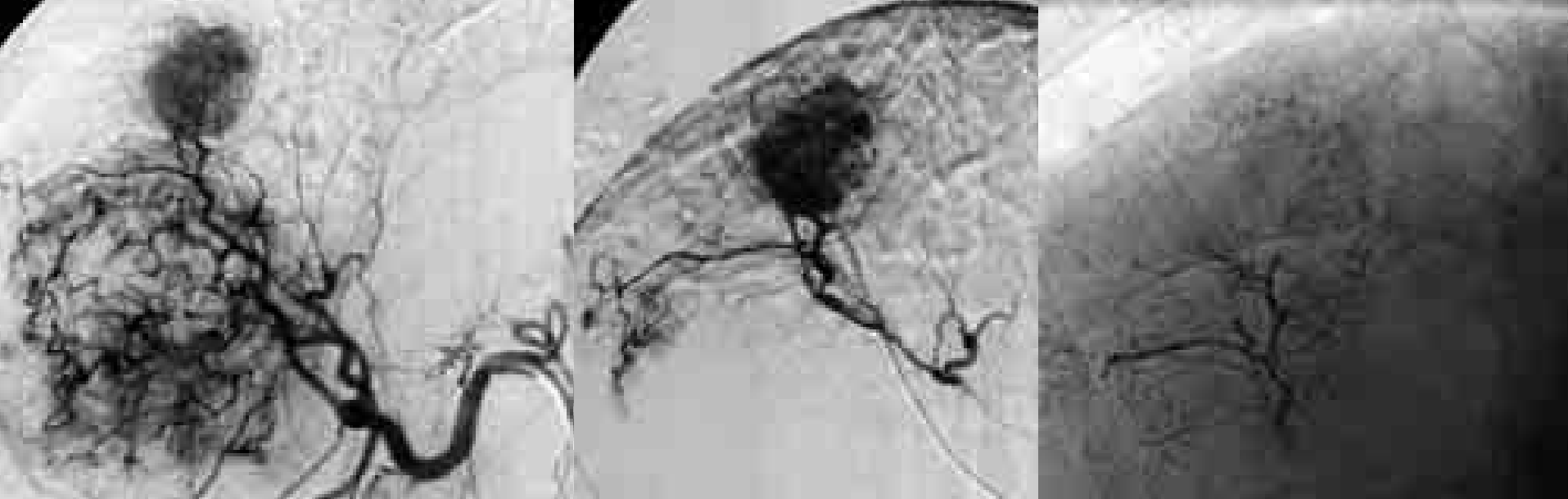
No single shot treatment

Experimental Liver Embolization

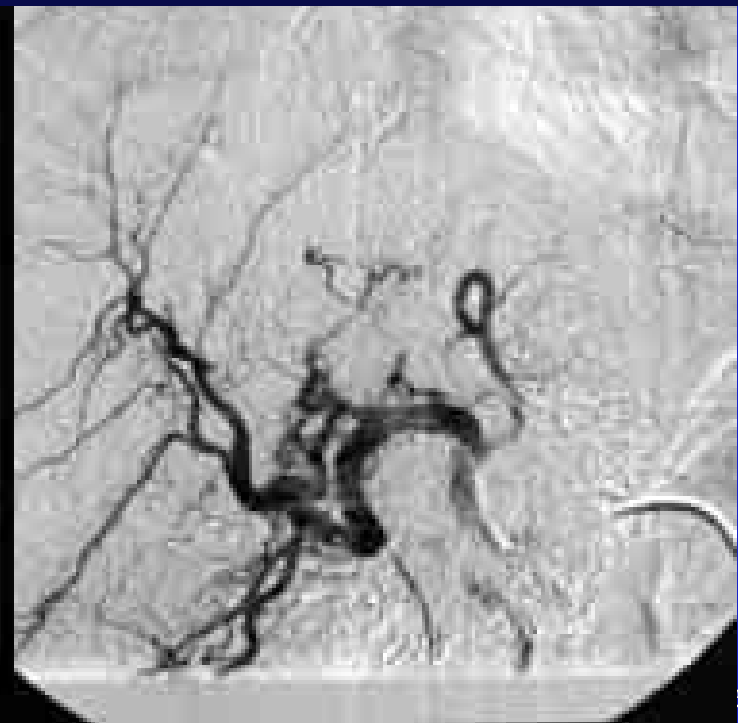
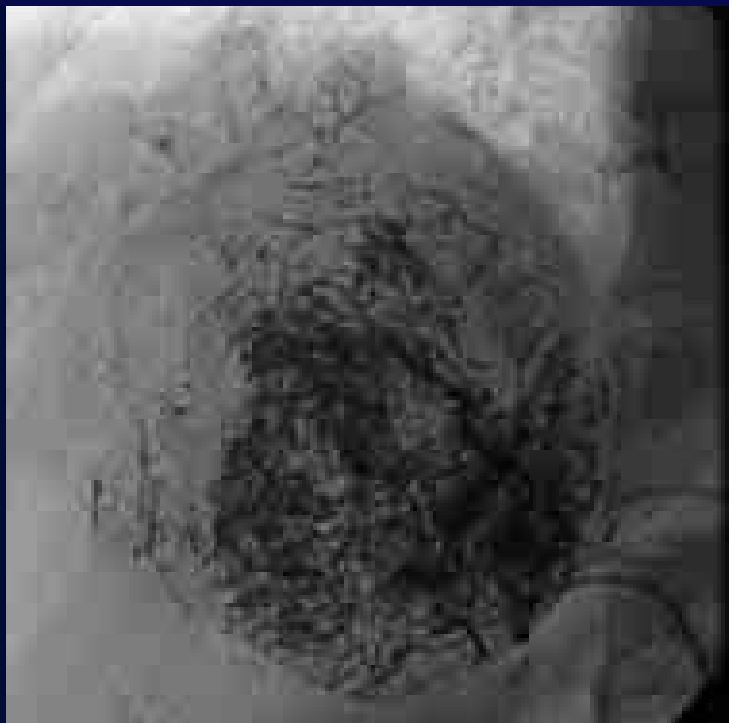
1 week follow-up

4 weeks follow-up





3 sessions: Lipiodol + Carboplatin + ultrasmall spheres



**Anticancer Res. 2006 Sep-
Oct;26(5B):3793-5.**

**Target Trans-arterial chemoembolization
(TACE) of liver metastases from
colorectal cancer using irinotecan-
eluting beads: preliminary results.**

**Aliberti C, Tilli M, Benea G,
Fiorentini G.**

**Conclusion: Irinotecan drug-eluting
beads administered as TACE were
shown to be active and safe in
patients with liver metastases from
CRC.**

Drug Delivering Beads for Embolization

*Symposium
CIRSE 2004*

1.15 - 1.45pm

Sunday 20th September 2004

Auditorium Diagonal

Palau de Congressos, Barcelona

TERUMO



Biocompatibles

Drug Eluting Beads for HCC

	12 mo	24 mo
Precision TACE		
Malagari	98%	91%
Valela	93%	89%
Conventional TACE		
Llovet	82%	63%
Pelletier	24%	15%
Our technique	91%	

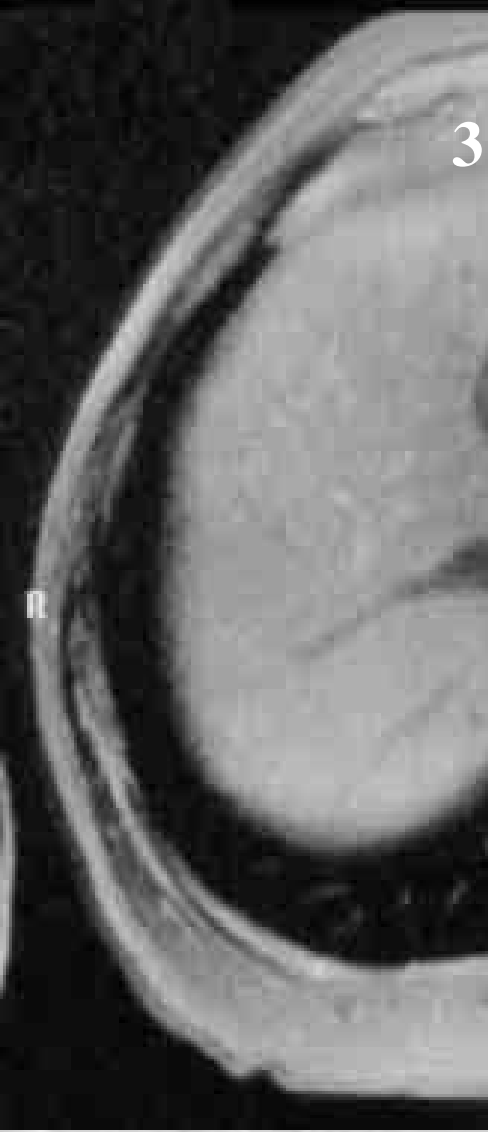
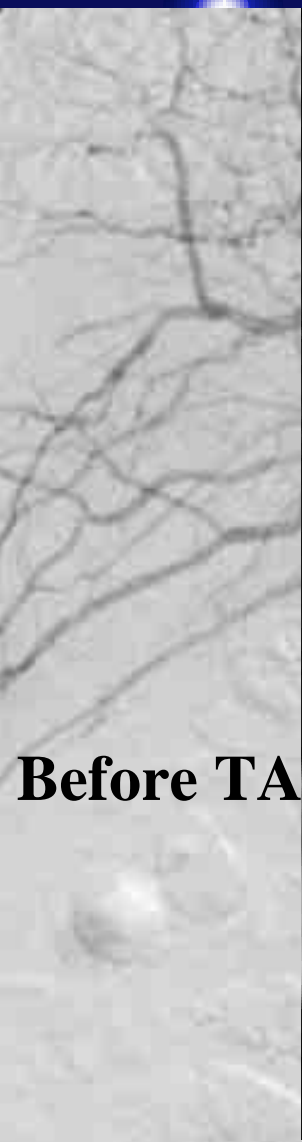
The Biosphere Approach

HepaSphere®: hepatic artery embolization in a porcine model

E. de Luis, et al. CIRSE 2005 Presentation Number: 47.2.2

Conclusion: Hepasphere® occluded the hepatic arteries without damaging portal spaces structures and without inducing parenchymal necrosis. The vascular long-term occlusion and phagocytosis of the material by inflammatory cells may suggest the possibility of using Hepasphere® as a slow releaser drug-carrier for hepatocarcinoma treatment.

Limitations!



Limitations!



Options?

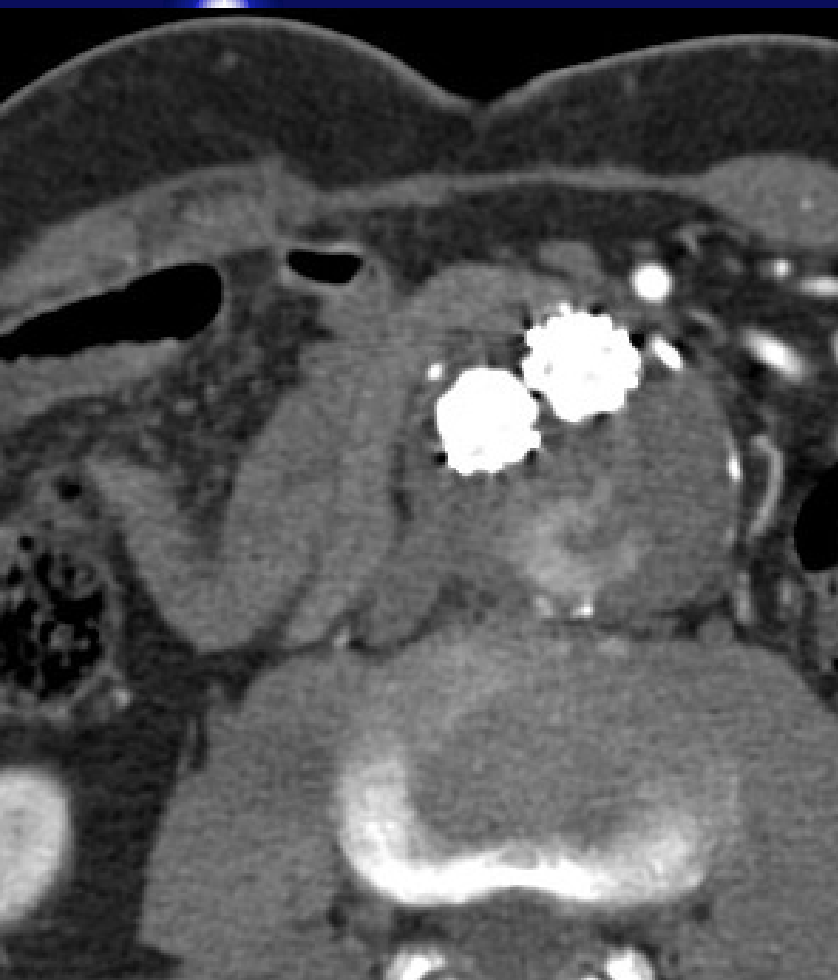
Clinical Background

Benign Tumors: UFE

Malignant Tumors: HCC, RCC

Vascular Disease: Endoleaks, AVM

Endoleaks and Embolization



Onyx

Treatment of Type II
Endoleaks with Onyx

Martin et al.

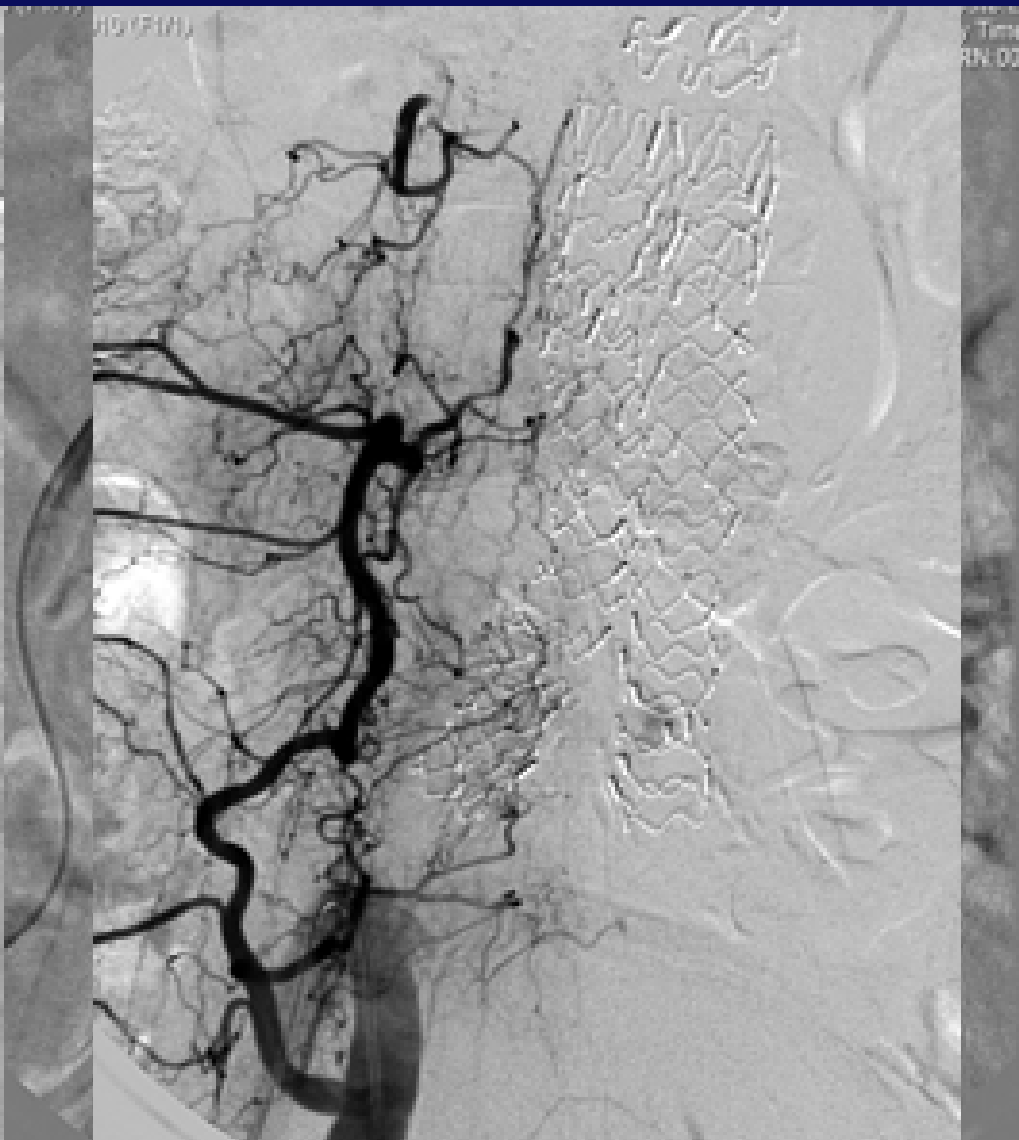
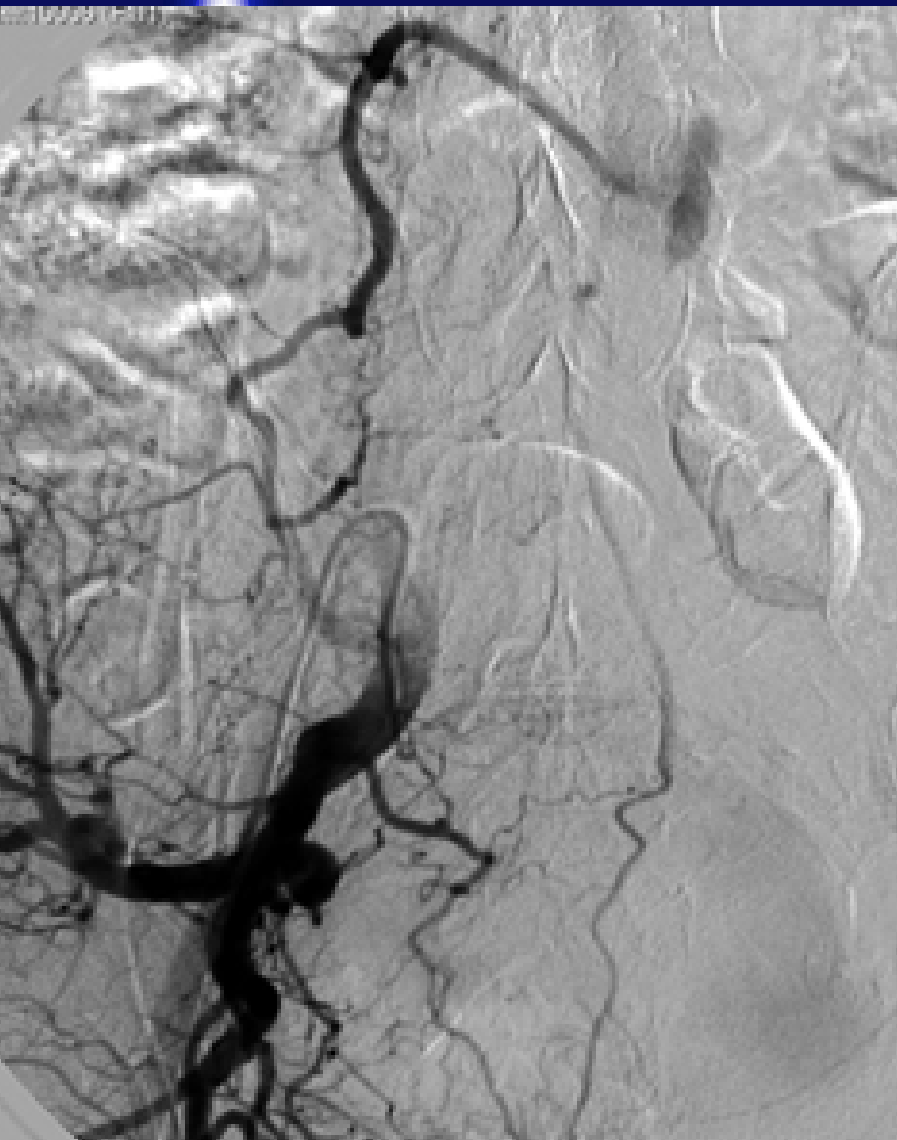
JVIR 2001;12:629



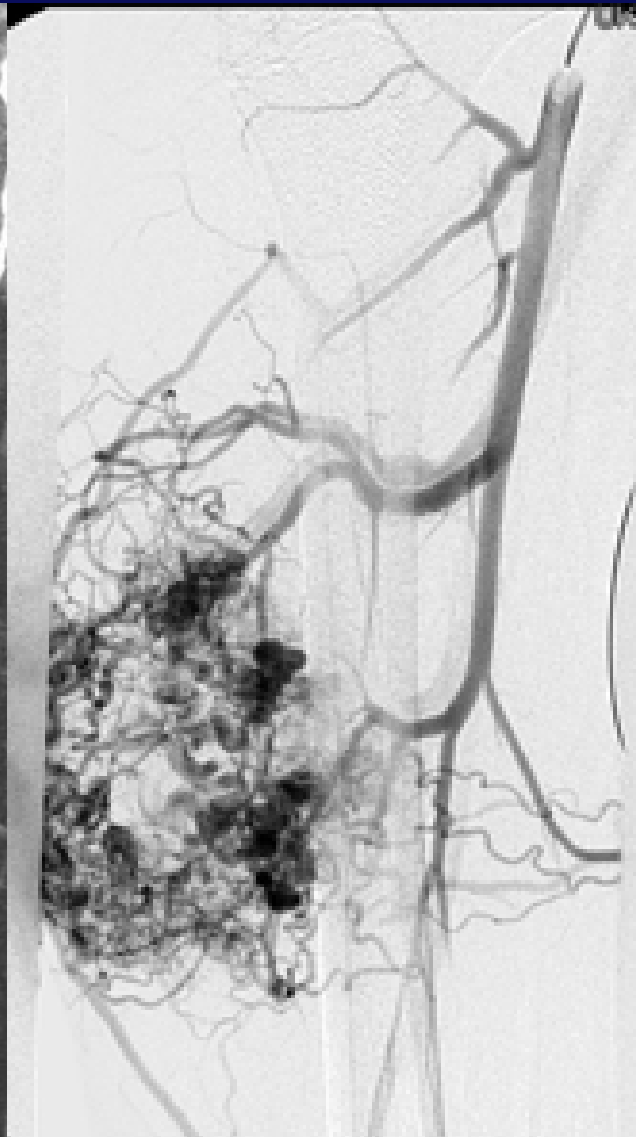
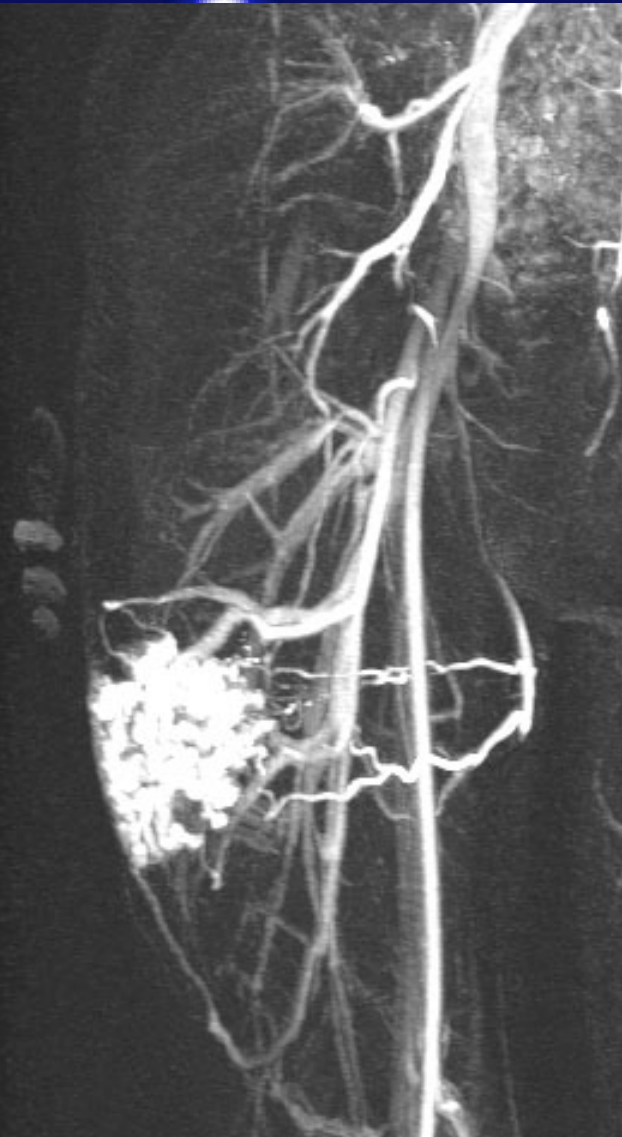
b.

d.

We prefer Ethibloc:



AVM: We prefer Ethibloc again



7.5 ml Ethibloc

Conclusion

In spherical materials mechanical integrity and biocompatibility dependant on design

In HCC progress/success only by multimodality concepts

Sophisticated liquid embolics for complex interventions

In Europe Ethibloc might be preferred because of cost effectiveness