



HepaSpheres Microspheres
Quality
Targeted to the tumor
Absorbs drug
Conforms to the vessel
Elutes and embolizes

hqTACE

The Next Generation in
Liver Cancer Treatment

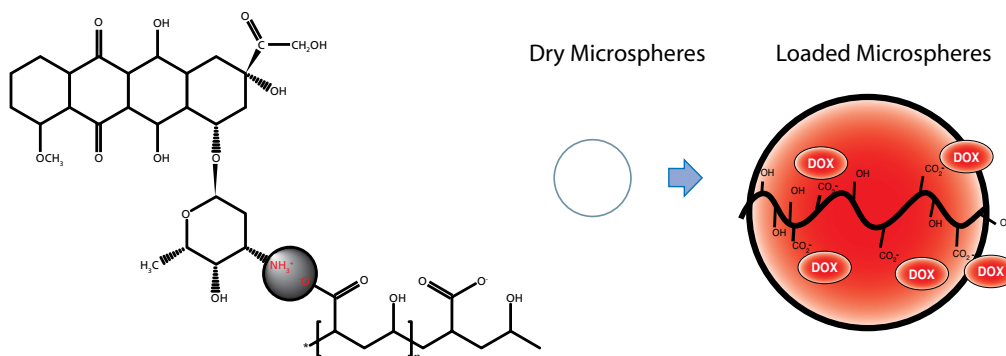


hqTACE – The No-Compromise Embolization and Delivery Solution

hqTACE provides calibrated sizing, efficient loading, effective drug delivery, and robust handling properties to help ensure effective treatment of the targeted tumor, and clinical confidence.

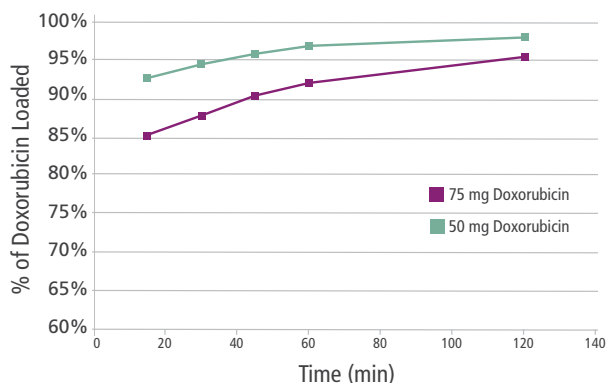
FEATURES	BENEFITS
Predictable sizing	Effective and reliable microsphere sizing for desired level of occlusion
Unique highly conformable composition	Increased intimal surface area contact for enhanced drug delivery and more complete occlusion for excellent embolic effect
Ability to load drug consistently throughout the entire sphere	Sustained delivery of chemotherapeutic agent
New enhanced preparation and drug-loading process	Easy delivery and dispersion after drug loading, with no catheter clogging
Poly(sodium acrylate vinyl alcohol) copolymer	Proven biocompatibility

HEPASPHERE MICROSPHERES MECHANISM OF LOADING WITH DOXORUBICIN

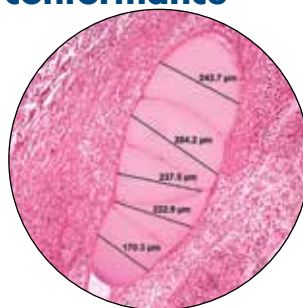


The doxorubicin is loaded and eluted by a reversible ionic exchange mechanism. The negatively charged acrylate of HepaSpheres Microspheres interacts with the positively charged doxorubicin hydrochloride.

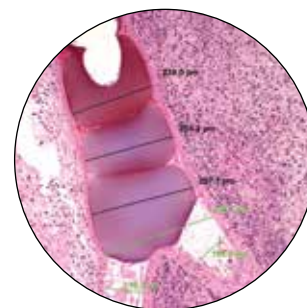
HEPASPHERE MICROSPHERES DOXORUBICIN LOADING PROFILE



More complete occlusion and excellent drug delivery result from greater intimal surface area contact and superior conformance²



HepaSphere Microspheres with doxorubicin 14 days post treatment



HepaSphere Microspheres with doxorubicin occluding a bifurcated vessel

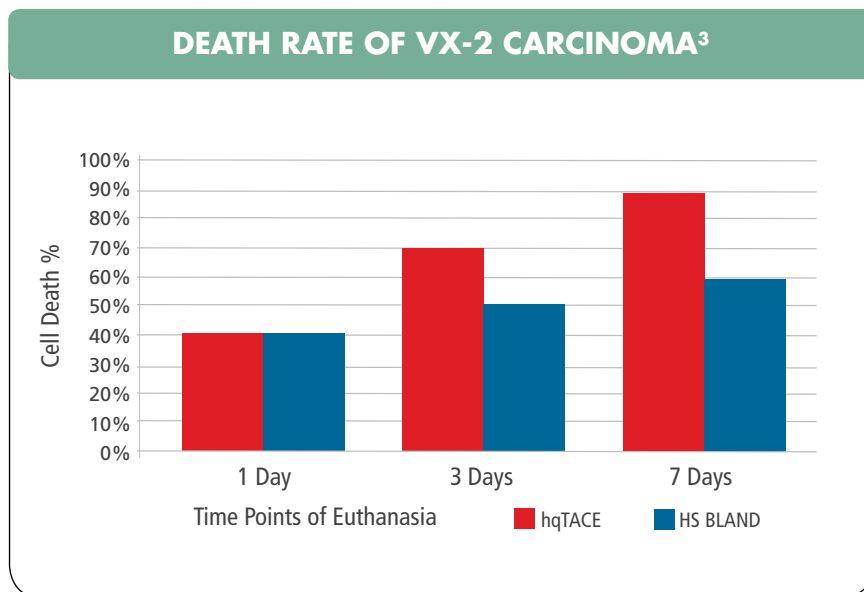
The Next Generation in Liver Cancer Treatment

In Vivo Animal Validation Studies Confirm Proof of Concept of Loading and Delivery Performance

hqTACE with HepaSphere Microspheres provides advanced performance characteristics for effective clinical outcomes.

Effective Cell Destruction Rate in Target Cancer Cells

Doxorubicin-loaded HepaSphere Microspheres achieved high rates of tumor necrosis in a VX-2 rabbit tumor model compared to bland embolization while maintaining low systemic drug exposure.



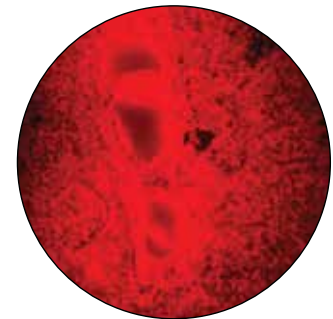
At seven days, the cell death rate in a VX-2 model was 90% with doxorubicin-loaded HepaSphere Microspheres and 60% with bland embolization using HepaSphere Microspheres

Effective Doxorubicin Delivery and Penetration

Fluorescence imaging confirms doxorubicin delivery and associated tissue penetration of up to 1600 microns into the surrounding tissue in a VX-2 rabbit tumor model within 24 hours following treatment.²

Uncompromised Embolic Performance

Animal studies confirm that HepaSphere Microspheres loaded with doxorubicin achieve the same mean level of occlusion as HepaSphere Microspheres used in bland embolization.²



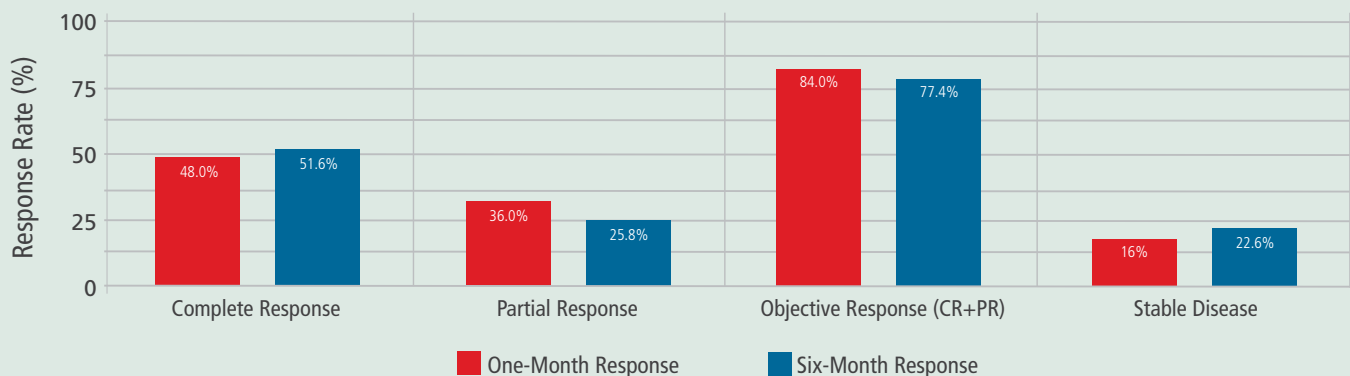
Clinical Experience: High Objective Tumor Response with Low Complications

Clinical experience with doxorubicin-loaded HepaSphere Microspheres validates preclinical studies demonstrating that hqTACE provides high efficacy with associated low systemic drug exposure. This minimizes the impact to underlying healthy liver function and other doxorubicin-related toxicity.

High Objective Tumor Response

A multicenter study followed 50 patients (36 males, 14 females, aged 54 to 80 years) with primary HCC and classified as Child-Pugh class A or B (92% Child-Pugh A). Patients were treated with HepaSphere Microspheres loaded with a dose of 50 mg doxorubicin or epirubicin. Objective tumor response was 77.4% at 6-month follow-up, as measured by mRECIST criteria.⁴

TUMOR RESPONSE AT 1 AND 6 MONTHS⁴



The **NEXT** Generation

Transarterial chemoembolization (TACE) is a standard of care for non-resectable hepatocellular carcinoma (HCC). Drug-delivery TACE—the use of an embolic material to load and deliver chemotherapeutic agents directly to the tumor—improves on conventional TACE by enabling higher drug concentration that is precisely targeted and delivered directly to the tumor site, resulting in fewer drug-related adverse events. A major advantage of drug-delivery TACE compared to conventional TACE is improved patient safety as a result of lower systemic doxorubicin circulation, resulting in less impact on normal liver function¹ during treatment.

Now, hqTACE (drug-delivery TACE with HepaSpheres Microspheres) is taking drug-delivery TACE to the next level. Manufactured by BioSphere Medical, S.A., the worldwide leader in microsphere technology, HepaSpheres Microspheres offer ease of handling, superior embolic performance, highly efficient drug loading/delivery and clinical effectiveness.

Consistent loading throughout the sphere offers potential for optimal drug loading and delivery.

Cross section of HepaSpheres Microspheres loaded with doxorubicin originally taken at 20X magnification. The red color indicates the presence of doxorubicin. Data on file at BioSphere Medical, Inc.

ORDERING INFORMATION

HepaSphere Microspheres

Size range of dry particles (µm)	Size range when expanded (µm)	Quantity (mg)	Order number
30-60	120-240*	1 vial, 25mg	V225HS
50-100	200-400*	1 vial, 25mg	V325HS
100-150	400-600*	1 vial, 25mg	V525HS
150-200	600-800*	1 vial, 25mg	V725HS

*When in contact with non-ionic contrast media or normal saline (NaCl 0.9%) HepaSphere Microspheres expand to 4X their dry state diameter. Please refer to the product IFU before product use.

Not all goods are available in every country.

REFERENCES

1. van Malenstein H, et al. A Randomized Phase II Study of Drug-eluting Beads versus Transarterial Chemoembolization for Unresectable Hepatocellular Carcinoma. *Onkologie* 2011; 34(7):368-76.
2. Gupta S, et al. Hepatic Arterial Embolization with Doxorubicin-Loaded Superabsorbent Polymer Microspheres in a Rabbit Liver Tumor Model. *Cardiovascular Interventional Radiology* 2011; Apr 9 DOI 10.1007 / 500270-011-0154-6.
3. Lee K, et al. Doxorubicin-Loaded QuadraSphere Microspheres: Plasma Pharmacokinetics and Intratumoral Drug Concentration in an Animal Model of Liver Cancer. *Cardiovascular Interventional Radiology* 2010; 33(3):576-82.
4. Grosso M, et al. Transarterial Chemoembolization for Hepatocellular Carcinoma with Drug-Eluting Microspheres: Preliminary Results from an Italian Multicentre Study. *Cardiovascular Interventional Radiology* 2008; 31(6):1141-49.



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