
DC Bead™
Made to a higher standard. Yours.
We don't make DC Bead™ for just anybody.
We make it for you. We make it for your patients.
Imagine where we can go.
BTG
btg-im.com

DC Bead™

Made to a higher standard. Yours.

The gold-standard drug-eluting bead, DC Bead™ is supported by ten years' experience and more than 80 publications reporting outcomes in over 3000 hepatocellular carcinoma (HCC) patients.[1]

The excellent performance characteristics of DC Bead™ are directly linked to its chemistry; never assume another product will give you the same results.

DC Bead™ is made to a higher standard. Yours.

DC Bead™ 2005-2015 10 YEARS of higher standards

Only DC Bead™ is backed by clinical studies and peer-reviewed data in HCC which demonstrate:

- ✓ Safety, efficacy and tolerability[2-4,6]
- ✓ Improved outcomes over conventional TACE[2-4,6-8]
- ✓ Improved outcomes over bland embolisation[9]
- ✓ Five-year survival data[10,11]
- ✓ Reproducibility of procedure[12]
- ✓ Promising outcomes in downstaging and bridge-to-transplant settings[13-15]
- ✓ Tolerability in patients receiving sorafenib[16]
- ✓ Encouraging health economic data[17]

DC Bead™ has earned your confidence

2005

2005 — FIRST Commercial Shipment of DC Bead™

2007 — FIRST Efficacy and Pharmacokinetic Data (HCC)[2,34]

2007 — FIRST Evidence of Efficacy in Asian Population (HCC)[3]

2010 — FIRST Commercial Shipment of DC Bead*M1*™

2010 — FIRST Randomised Controlled Trial: PRECISION V (HCC)[4,35]

2010 — FIRST Explant Data Animal Study (HCC)[5,34]

2012 — FIRST DEBDOX™ with DC Bead™: Expert Panel Technical Recommendations (HCC)[12,35]

2012 — FIRST Five-year Survival Data (HCC)[10,11,34,35]

2012

2014 — Positive Health Economic Data with DC Bead™[17]

2015 — Latest Evidence of Clinical Benefits vs cTACE (HCC)[6]

2015 — FIRST Safety and Efficacy of DC Bead*M1*™ including Bridge to Transplant (HCC)[15,35]

2015

The Science of DC Bead™ is Unique. The Performance of DC Bead™ is Unique.

DC Bead™

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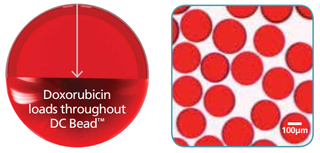
Confidence in CE Mark Approval for Drug Loading



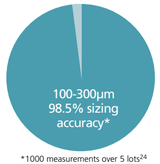
Doxorubicin-loaded DC Bead™

- Homogeneous drug loading with distribution throughout DC Bead™[18,19,20]
- Peer-reviewed 14-day storage and stability data, supported by robust microbiological testing[21,22,23]

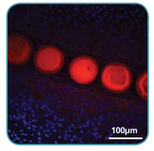
Only DC Bead™ has loading of doxorubicin and irinotecan within its CE Marked indication statement

+

Confidence in Targeted, Predictable Embolisation



*1000 measurements over 5 lots[24]



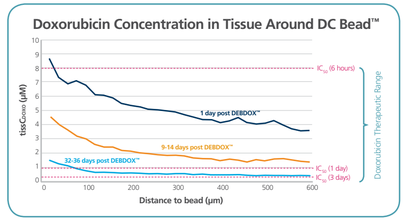
Precisely calibrated DC Bead™ in vessel

- All DC Bead™ are > 95% within labelled size range[24]
- Unique compressibility – with no fragmentation or aggregation – protects spherical integrity for effective embolisation[26,18]
- Histological research confirms correlation between labelled size and vessels embolised[27]

Only DC Bead™ has peer-reviewed data supporting structural integrity and label-to-vessel size correlation[18,27]

+

Confidence in Sustained and Controlled Drug Delivery



Graph adapted from: Namur J et al. J Hepatol 55 (2011): 1332-1338

- Sustained release of doxorubicin into the tumour from DC Bead™ at therapeutically meaningful levels for over 30 days[27]
- Diffusion of the eluted doxorubicin over a distance of 1.2mm from the occluded vessels[27]

Only DC Bead™ has histological data to support sustained doxorubicin elution in vivo[27]

=

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- ✓ Tolerability in patients receiving sorafenib[16]
- ✓ Encouraging health economic data[17]

DC Bead™ has earned your confidence

2005

2005 FIRST Commercial Shipment of DC Bead™

2006 FIRST In-vivo Evidence of Dose Delivery to Tumour with Low Systemic Exposure[25]

2007 FIRST Efficacy and Pharmacokinetic Data (HCC)[2,34]

2007 FIRST Evidence of Efficacy in Asian Population (HCC)[3]

2010 FIRST Evidence vs Bland Embolisation (HCC)[9]

2010 FIRST Commercial Shipment of DC Bead*M1*™

2010 FIRST Randomised Controlled Trial: PRECISION V (HCC)[4,35]

2010 FIRST Explant Data Animal Study (HCC)[5,34]

2011 FIRST Data in Patients Receiving Sorafenib (HCC)[16]

2011 FIRST Clinical Explant Data (HCC)[7,34]

2012 CE Mark Approval for DC Bead*M1*™ Loaded with Doxorubicin

2012 FIRST Benefits of 70-150um Size Distribution[28,34]

2012 FIRST DEBDOX™ with DC Bead™: Expert Panel Technical Recommendations (HCC)[32,35]

2012 FIRST Five-year Survival Data (HCC)[10,11,34,35]

2012

2014 Positive Health Economic Data with DC Bead™[17]

2015 Latest Evidence of Clinical Benefits vs cTACE (HCC)[8]

2015 FIRST Safety and Efficacy of DC Bead*M1*™ including Bridge to Transplant (HCC)[15,35]

2015

DC Bead™: The Gold Standard for Dose Delivery and Toxicity Management

Early trials validated the highly targeted drug-delivery properties of DC Bead™

≥ 11.5 x more doxorubicin to the tumour[25]

Hong et al 2006

DEBDOX™ with DC Bead™ vs cTACE

> 96% reduction in systemic exposure peak concentration Cmax[2] **(p=0.00002)**

Varela et al 2007

> 60% reduction in doxorubicin in plasma AUC[2] **(p=0.001)**

Varela et al 2007

"The better profile of DEBTACE vs conventional TACE opens the opportunity to increase the amount of drug selectively exposed to tumor cells and simultaneously, reduce toxicity."

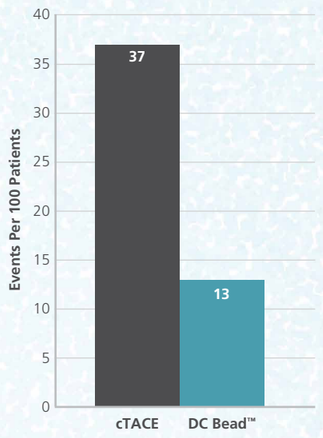
Varela et al. J Hepatol 46 (2007): 474-481

The PRECISION V randomised controlled trial demonstrated the important patient benefits of DEBDOX™ with DC Bead™, with highly significant reductions vs cTACE in:

- Toxicity to healthy liver ($p < 0.001$)[4] with lower increases in transaminase enzyme levels after each of three treatments
- Frequency of doxorubicin-related adverse events ($p < 0.0001$)[4] despite receiving 30% higher dose of doxorubicin

In PRECISION V, DEBDOX™ with DC Bead™ improved response in all treated patients, and showed significant improvement ($p < 0.05$) in more fragile patients, without compromising tolerability[4]

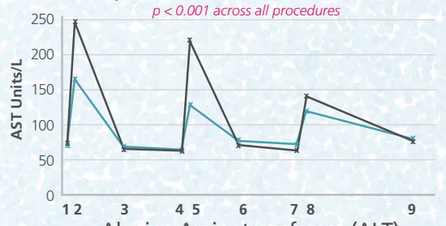
Improved Tolerability: Doxorubicin-Related Side Effects[4]



Protection of Healthy Liver: Liver Enzyme Levels[4]

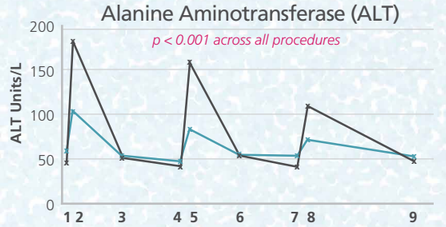
Aspartate Aminotransferase (AST)

p < 0.001 across all procedures



Alanine Aminotransferase (ALT)

p < 0.001 across all procedures

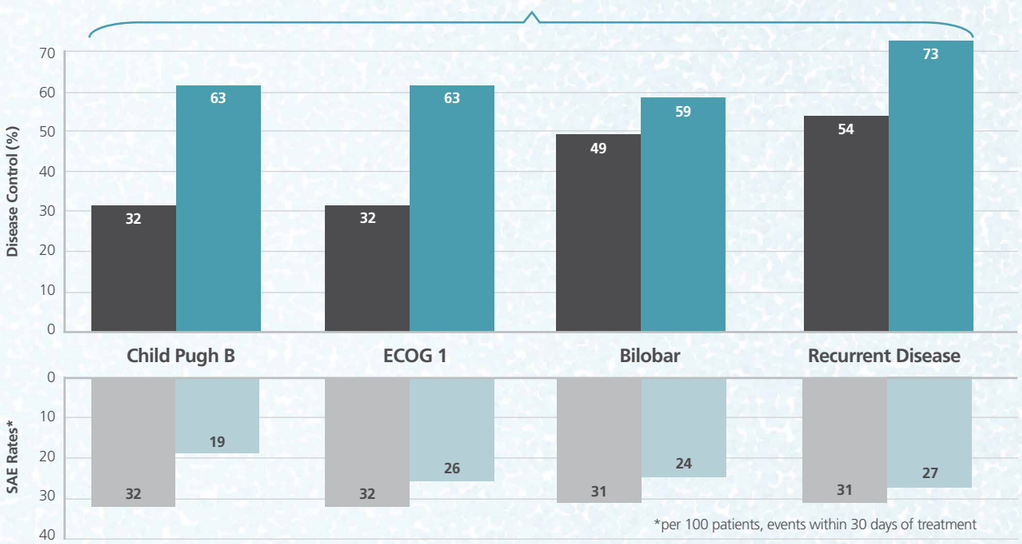


Timepoint

1: T1 Pre emb (LOCF)
2: T1 Pre discharge
3: 1 month
4: T2 Pre emb
5: T2 Pre discharge
6: 3 months
7: T3 Pre emb
8: T3 Pre discharge
9: 6 months

DEBDOX™ with DC Bead™ in Advanced Patients[4]

Objective Response (p=0.038) and Disease Control (p=0.026)



*per 100 patients, events within 30 days of treatment

Graphs adapted from: Lammer J et al. Cardiovasc Intervent Radiol. 2010 Feb; 33(1): 41-52

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DC Bead M1™

DC Bead™: Setting New Standards in the Treatment of Unresectable HCC

The benefits of DC Bead™ are now recognised in the European Clinical Practice Guidelines for HCC.[29,30]

Clinical Practice Guidelines

EASL EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER | JOURNAL OF HEPATOLOGY

EASL–EORTC Clinical Practice Guidelines: Management of hepatocellular carcinoma

European Association for the Study of the Liver,
rch and Treatment of

Chemoembolization is recommended for patients with BCLC stage B, multinodular asymptomatic tumors without vascular invasion or extra hepatic spread (evidence 1iiA; recommendation 1A).

The use of drug-eluting beads has shown similar response rates than gelfoam-lipiodol particles associated with less systemic adverse events (evidence 1D; recommendation 2B).

clinical practice guidelines

Annals of Oncology 23 (Supplement 7): vii41–vii48, 2012
doi:10.1093/annonc/mds225

Hepatocellular carcinoma: ESMO–ESDO Clinical Practice Guidelines for diagnosis, treatment and follow-up

C. Verslype, O. Rosmorduc & P. Rougier, on behalf of the ESMO Guidelines Working Group

TACE is recommended for patients with HCC BCLC stage B, or those with an excellent liver function and multinodular asymptomatic tumors without macroscopic vascular invasion or extra-hepatic spread [I, A].

Studies with doxorubicin-eluting beads (DEBDOX™) have demonstrated less systemic leakage of chemotherapy in the systemic circulation, resulting in less side effects, with at least the same activity in randomized phase II trials with conventional TACE (gelfoamlipiodol particles) as comparator. TACE with selective administration with doxorubicin-eluting beads is an option to minimize systemic side effects of chemotherapy [II, A].

DC Bead™ is challenging survival expectations for intermediate HCC patients.[10,11]

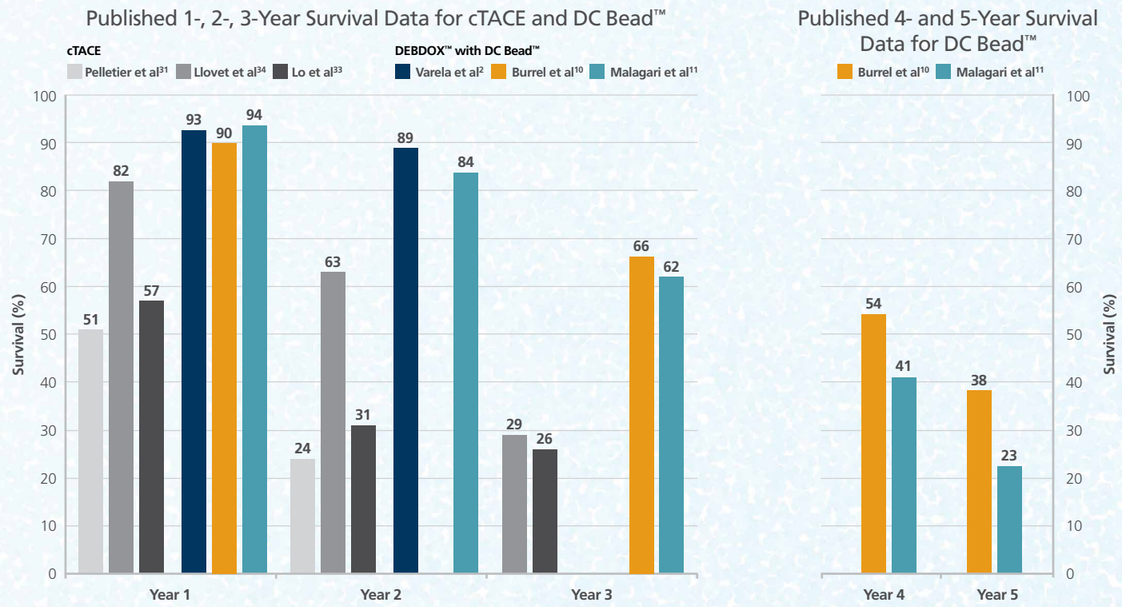
Overall, the median survival for intermediate HCC cases is expected to be around 16 months, whereas after chemoembolization the median survival is about 20 months.

Median overall survival unresectable HCC
48.6 months[10*]
54.2 months BCLC A
47.7 months BCLC B

*95% CI: 36.9-61.2. Median survival after censoring follow-up at the time of transplant (n=2), sorafenib treatment (n=24) or radioembolisation (n=1) was 47.7 months (96% CI: 37.9-57.5)

Median overall survival unresectable HCC
43.8 months[11]
48.7 months Child class A
36.7 months Child class B

Published 1-, 2-, 3-Year Survival Data for cTACE and DC Bead™



Published 4- and 5-Year Survival Data for DC Bead™

Note: These studies had different patient populations and study designs and therefore are not directly comparable

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DC Bead M1™

DC Bead™

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DESCRIPTION

DC Bead™ and DC Bead*M1*™ comprise a range of hydrogel microspheres that are biocompatible, hydrophilic, non-resorbable, and precisely calibrated. They are CE Mark approved for loading with doxorubicin and irinotecan which is released in a controlled manner after embolisation. DC Bead™ and DC Bead*M1*™ are produced from polyvinyl alcohol and are blue-tinted to aid with visualisation during preparation and loading.

PRESENTATION

- Single-unit pack
  - 10ml vial containing 2ml beads in physiological buffered saline solution (total volume approx 8ml)
  - Each vial stopper-sealed with an aluminium cap and colour-coded lid
- Four-year shelf-life from date of manufacture
- Steam sterilised

INDICATIONS

DC Bead™ is intended to be loaded with doxorubicin for the purpose of:

- Embolisation of vessels supplying malignant hypervascularised tumour(s)
- Delivery of a local, controlled, sustained dose of doxorubicin to the tumour(s)

DC Bead™ is also intended to be loaded with irinotecan for the purpose of:

- Embolisation of vessels supplying malignant colorectal cancer metastasised to the liver (mCRC)
- Delivery of a local, controlled, sustained dose of irinotecan to the mCRC

Both products and/or all indications may not be available in your territory. DC Bead™ and DC Bead*M1*™ are not cleared by the FDA for sale or distribution in the USA. For full instructions for use, please visit www.dcbead.com/ifu and www.dcbeadm1.com/ifu

DC Bead*M1*™

Physical and chemical stability of drug-loaded DC Bead™	
Doxorubicin-loaded DC Bead™ (75mg/2ml)	14 days (at 2-8°C)
Doxorubicin-loaded DC Bead™ mixed with non-ionic contrast media	7 days (at 2-8°C)
Irinotecan-loaded DC Bead™ (100mg/2ml)	14 days (at 2-8°C)
Irinotecan-loaded DC Bead™ mixed with non-ionic contrast media	Use immediately

DC Bead*M1*™ is primarily intended as an embolic agent to treat vessels supplying malignant colorectal cancer metastasised to the liver (mCRC) and malignant hypervascularised tumour(s).

- DC Bead*M1*™ is compatible with irinotecan, which can be loaded prior to embolisation and then, as a secondary action, elute a local, controlled and sustained dose to the mCRC after embolisation
- DC Bead*M1*™ is also compatible with doxorubicin, which can be loaded prior to embolisation and then, as a secondary action, elute a local, controlled and sustained dose to the tumour after embolisation

DC Bead™

"Although further confirmation of our findings with randomized controlled trials is warranted, our report seems to indicate that the use of DEB-TACE in LT recipients with HCC can increase recurrence-free survival after liver transplantation."

Nicolini D et al. World J Gastroenterol 19 (2013): 5622-32

"In conclusion, in patients with HCC, TACE with DEB offered better safety and efficacy profiles compared to TACE using gelatin sponges or TACE with microspheres."

Liu et al. Korean J Radiol 16 (2015): 125-32

"These data validate the safety of DEB-TACE and show that the survival expectancy applying current selection criteria and technique is better than that previously reported."

Burrel M, Reig M, Forner A et al. J Hepatol 56 (2012): 1330-1335

"The survival rates of patients with Child class B disease are quite high in our study, a fact that is in accordance with the findings of the Precision V study, which showed that patients with more advanced liver disease had a significantly better local response."

Malagari K et al. Cardiovasc Interv Radiol 35 (2012): 1119-28

"Doxorubicin-loaded DC Bead™ provides levels of consistency and repeatability not available with conventional TACE and offers the opportunity to implement a standardized approach to HCC treatment."

Expert Panel. Cardiovasc Intervent Radiol 35 (2012): 980-5

DC Bead*M1*™

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  - 10ml vial containing 2ml beads in physiological buffered saline solution (total volume approx 8ml)
  - Each vial stopper-sealed with an aluminium cap and colour-coded lid
- Four-year shelf-life from date of manufacture
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- Delivery of a local, controlled, sustained dose of irinotecan to the mCRC

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DC Bead™ and DC Bead*M1*™ Important Safety Information:

Cautions: DC Bead™ and DC Bead*M1*™ :

- Embolisation with DC Bead™ and DC Bead*M1*™ should only be performed by a physician with appropriate interventional occlusion training in the region intended to be embolised
- Do not use if the vial or packaging appear damaged. Ensure that DC Bead™/DC Bead*M1*™ is an appropriate size for the intended vasculature
- Consider upsizing to a larger size of DC Bead™ in the presence of AV shunts or if angiographic evidence of embolisation does not appear quickly during delivery
- Consideration should be given to Tc99m-MAA scanning if there is suspicion of AV shunting

Potential Complications: DC Bead™/DC Bead*M1*™:

- Undesirable reflux or passage of DC Bead™/DC Bead*M1*™ into normal arteries adjacent to the targeted lesion or through the lesion into other arteries or arterial beds
- Non-target embolisation
- Pulmonary embolisation
- Ischaemia at an undesirable location
- Capillary bed saturation and tissue damage
- Ischaemic stroke or ischaemic infarction
- Vessel or lesion rupture and haemorrhage
- Neurological deficits including cranial nerve palsies
- Vasospasm
- Death
- Recanalisation
- Foreign body reactions necessitating medical intervention
- Infection necessitating medical intervention
- Clot formation at the tip of the catheter and subsequent dislodgement causing arterial thromboembolic sequelae

Cautions: Doxorubicin-loaded DC Bead™/DC Bead*M1*™:

- Exceeding a loading dose of 37.5mg doxorubicin per 1ml DC Bead™/DC Bead*M1*™ may lead to some systemic distribution of doxorubicin and related side effects

Cautions: Irinotecan-loaded DC Bead™/DC Bead*M1*™:

- On addition of contrast/water mixture to loaded beads some irinotecan will be eluted. On delivery a bolus of between 10-20mg irinotecan may be delivered
- Do not use irinotecan-loaded beads with contrast agents containing salts (eg calcium chloride)
- The maximum amount of irinotecan that can be loaded is 100mg irinotecan per 2ml vial of DC Bead™/DC Bead*M1*™
- Exceeding this amount may lead to some irinotecan remaining free in solution. This free solution should be removed prior to use to prevent the patient receiving the excess dose as a bolus

DC Bead™

"DEBDOX™/DC BeadM1™ TACE is an effective procedure with a favorable safety profile and promising results in terms of objective response rate, tumor downstaging and necrosis."

Spreafico C et al. Cardiovasc Intervent Radiol 38 (2015): 129-34

"The main hypothesis to explain the cost difference between the two periods is that the strategy with the possibility of using DEBs was significantly associated with fewer hospitalizations for the management of toxicity and with shorter overall hospital stays."

Vadot L et al. J Clin Pharm Ther 40 (2015): 83-90.

"These data validate the safety of DEB-TACE and show that the survival expectancy applying current selection criteria and technique is better than that previously reported."

Burrel M, Reig M, Forner A et al. J Hepatol 56 (2012): 1330-1335

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DC Bead *M1*™

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ORDERING INFORMATION

	DC Bead*M1*™	DC Bead™		
Size	70-150µm	100-300µm	300-500µm	500-700µm
Label Colour	Black and yellow	Yellow	Blue	Red
Volume of Beads	2ml	2ml	2ml	2ml
Product Code	DC2V001	DC2V103	DC2V305	DC2V507

DC Bead™ and DC Bead*M1*™ are manufactured by:
Biocompatibles UK Limited
a BTG International group company
Chapman House, Farnham Business Park
Weydon Lane, Farnham, Surrey
GU9 8QL, UK

OUR BTG CUSTOMER SERVICES TEAM: customer.services@btgplc.com

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FRANCE	tel. +33-184884056
GERMANY	tel. +49-3030809275
IRELAND	tel. +353-15134139
ITALY	tel. +39-0694805067
NETHERLANDS	tel. +31-202410932
PORTUGAL	tel. +351-308802698
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