DC Bead™ has been shown to produce high response rates with a very favourable safety profile in HCC, cholangiocarcinoma, neuroendocrine metastases and colorectal metastases. Furthermore, data produced by the same authors in treatment of colorectal cancer provide further evidence that supports the use of DC Bead™ in this indication.

Data also show that patient selection may be a key factor in ensuring optimal results. In the case of primary liver cancer, patients with advanced stages of cirrhotic and/or cancer disease were excluded from treatment. For metastatic disease, patients with a high degree of extrahepatic disease, a very high liver involvement and/or liver failure were also excluded from treatment.

The evidence from these data supports the use of DC Bead™ for treatment of primary and secondary liver cancer. Owing to limited data and heterogeneity of studies for indications outside HCC, further trials are required in order to confirm these results. In the meantime, and given the poor prognosis and limited efficacy of existing therapies for these malignancies, DC Bead™ should be considered as a treatment option, provided the patient is a good candidate for such therapy.
Following the results from the randomised PRECISION V trial, DC Bead™ Drug-Eluting Bead doxorubicin [DEBDOX™] (Biocompatibles UK) is becoming widely accepted as a ‘standard’ TACE treatment for patients with intermediate HCC. As the benefits of DEBDOX™ in the treatment of HCC become clearer, interest is increasing in defining the role of this innovative technology in the treatment of other liver malignancies.

Three recent publications have studied the role of DC Bead™ in the treatment of primary and secondary liver cancer. In a review by Carter & Martin, DC Bead™ treatment for both these indications is evaluated, while two other publications refer to single-arm studies for the use of DC Bead™ Drug-Eluting Bead irinotecan [DEBIRI™] for the treatment of liver metastases from colorectal cancer.

**Drug-eluting bead therapy in primary and metastatic disease of the liver**


### ABSTRACT

**Background:** Drug-eluting bead transarterial chemoembolization (DEB-TACE) [DEBDOX™] is a novel therapy for the treatment of hypervascularized tumours. Through the intra-arterial delivery of microspheres, DEB-TACE allows for embolization as well as local release of chemotherapy in the treatment of hepatic malignancy, providing an alternative therapeutic option in unresectable tumours. Its role as an adjunct to surgical resection or radiofrequency ablation (RFA) is less clear. The purpose of this review is to summarize recent studies investigating DEB-TACE in order to better define safety, efficacy and outcomes associated with its use.

**Methods:** A systematic review of all published articles and trials identified nine clinical trials and 23 abstracts. These were reviewed for tumour histology, stage of treatment, delivery technique, outcome at follow-up, complications and mortality rates.

**Results:** Publications involved treatment of hepatocellular carcinoma (HCC), metastatic colorectal carcinoma (MCRC), metastatic neuroendocrine (MNE) disease and cholangiocarcinoma (CCA). Using Response Evaluation Criteria in Solid Tumours (RECIST) or European Association for the Study of the Liver (EASL) criteria, studies treating HCC reported response rates of 5% (5/101) at 1 month, 9% (8/91) at 4 months, 14% (19/138) at 6 months and 25% (2/8) at 10 months. Partial response (PR) was reported as 58% (76/131) at 1 month, 50% (67/119) at 4 months, 57% (62/108) at 5–7 months and 63% (5/8) at 10 months. Studies involving MCRC, CCA and MNE disease were less valuable in terms of response rate because there is a lack of comparative data. The most common procedure-associated complications included fever (46–72%), nausea and vomiting (42–47%), abdominal pain (44–80%) and liver abscess (2–3%). Rather than reporting individual symptoms, two studies reported rates of postembolic syndrome (PES), consisting of fever, abdominal pain, and nausea and vomiting, at 82% (75/91). Six of eight studies reported length of hospital stay, which averaged 2.3 days per procedure. Morbidity was reported as occurring in 10 of 456 (2%) procedures, or 10 of 214 (5%) patients.

**Conclusions:** Drug-eluting bead TACE is becoming more widely utilized in primary and liver-dominant metastatic disease of the liver. Outcomes of success must be expanded beyond response rates because these are not a reliable surrogate for progression-free survival or overall survival. Ongoing clinical trials will further clarify the optimal timing and strategy of this technology.

### REVIEW

In this article by Carter & Martin, the authors describe a systematic review carried out in February 2009 of all available literature for DC Bead™. The review included eight papers published in peer-reviewed journals and 19 abstracts. Of the eight published clinical trials, four involved HCC patients, two metastatic colorectal patients, one cholangiocarcinoma and one neuroendocrine disease. Results from these publications are summarised in the table opposite.

The authors of this review conclude that DEBDOX™ produces beneficial tumour response with an exceptionally low complication rate. In their view, this treatment has the potential to become an effective alternative therapy or palliative measure in the treatment of hepatic malignancy. They also highlight the need for standardisation across both DEBDOX™ technique and data collection.

### QUORUM Algorithm of Review of the DC Bead™ Publications and Abstracts

- **Potentially relevant publications identified and screened for retrieval** *n = 500*
- **Publications retrieved for more detailed evaluation** *n = 8*
- **Potentially appropriate publications to be included in the review** *n = 8*
- **Publications included in review** *n = 8*
- **RCTs with usable information, by outcome** *n = 8*
- **RCTs excluded n = 482**
  - List reasons
  - *n = Did not use DC Bead™*
- **Abstracts retrieved for more detailed evaluation** *n = 19*
- **Abstracts appropriate for review** *n = 19*
- **RCT, randomised controlled trial**

Table adapted from Carter S, and Martin RCG, HPB (Oxford) 11 (2009): 541-550

“The authors of this review conclude that TACE with DC Bead™ produces beneficial tumour response with an exceptionally low complication rate.”
### Inclusion Criteria
- HCC confirmed by EASL or biopsy
- Not suitable for resection, transplantation or PEI (except for 1 study)

### Exclusion Criteria
- BRB higher than 3mg/dl
- Advanced HCC
- Contraindication for embolisation
- Renal failure
- Severe atheromatosis

### Inclusion Criteria
- Histologically confirmed colorectal carcinoma, with metastatic disease confirmed by CT scan
- Karnofsky ≥60% or WHO PS 0-2
- Previous chemotherapy discontinued at least 4 weeks prior to beginning the study
- No signs of infection or ascites

### Exclusion Criteria
- Any history of inflammatory bowel disease or previous extensive bowel resection
- Signs of cardiac disease or renal, bone marrow, pulmonary or central nervous system metastases
- Uncontrollable infections
- Other types of cancer (except treated in situ cervical, basal cell carcinoma or squamous cell carcinoma)
- One study excluded patients with prior treatment with topoisomerase inhibitors

### Inclusion Criteria
- Histologically proven disease with 2 or fewer mitoses per high-powered field, and proven progressive disease on 2 subsequent imaging studies according to RECIST criteria
- BRB <2 x ULN
- Transaminases <3 x ULN
- Creatinine levels <120mol/l
- PT <1.5 IU
- Platelets >10^6/mm^3

### Exclusion Criteria
- Patients with any resectable disease
- Predominant extrahepatic disease
- Biliary tract dilatation, bilioenteric anastomosis or biliary stent
- Crossing the ampulla of Vater
- Previous treatment with TACE

### Treatment
**HCC**
- Doxorubicin used in all articles and most abstracts
- Doxorubicin doses from 25mg/m² up to a maximum dose of 150mg/m² per treatment

**Colorectal**
- Irinotecan at doses of 100mg per TACE procedure

**NET**
- Doxorubicin

**CholangioK**
- Doxorubicin

### Response Rates
**HCC**
- EASL: Overall Response 75% at 6M and 88% at 10M
- RECIST: Overall Response 42% at 6M

**Colorectal**
- RECIST: Overall Response 80% at 1M

**NET**
- RECIST: Overall Response 80% at 3M

**CholangioK**
- RECIST: Overall Response 100% at 3M

### Safety
- Fever (85% patients) reported
- Nausea and vomiting (93% patients) in ≥5%
- Abdominal Pain (80% patients)

### Length of Stay
- Average 2.3 days

### Mortality
- 11/233 (5%) patients - 5 of these 11 patients died from progressive disease

---

### Data for Published Studies Reviewed (n = 8)

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Date</th>
<th>Histology</th>
<th>Patients (n)</th>
<th>Chemotherapy Agent</th>
<th>Response Rate Reported</th>
<th>Complications Reported</th>
<th>Survival Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malagari et al</td>
<td>Nov 2007</td>
<td>HCC</td>
<td>71</td>
<td>Doxorubicin</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Poon et al</td>
<td>Sep 2007</td>
<td>HCC</td>
<td>35</td>
<td>Doxorubicin</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Aliberti et al</td>
<td>Oct 2006</td>
<td>MCRC</td>
<td>10</td>
<td>Irinotecan</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Fiorentini et al</td>
<td>Nov 2007</td>
<td>MCRC</td>
<td>20</td>
<td>Irinotecan</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Aliberti et al</td>
<td>July 2008</td>
<td>CAC</td>
<td>20</td>
<td>Doxorubicin</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Varela et al</td>
<td>March 2007</td>
<td>HCC</td>
<td>27</td>
<td>Doxorubicin</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>de Baere et al</td>
<td>June 2008</td>
<td>NE</td>
<td>20</td>
<td>Doxorubicin</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Ketterbach et al</td>
<td>Jan 2007</td>
<td>HCC</td>
<td>30</td>
<td>Doxorubicin</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**HCC**, hepatocellular carcinoma; MCRC, metastatic colorectal cancer; CAC, cholangiocarcinoma; NE, neuroendocrine disease

Table adapted from Carter S, and Martin RCG, HPB (Oxford) 11 (2009): 541-550
**Transarterial chemoembolization (TACE) using irinotecan-loaded beads for the treatment of unresectable metastases to the liver in patients with colorectal cancer: an interim report.**


---

**ABSTRACT**

**Background:** Following failure of standard systemic chemotherapy, the role of hepatic transarterial therapy for colorectal hepatic metastasis continues to evolve as the experience with this technique matures. The aim of this study was to gain a better understanding of the value of drug eluting bead therapy when administered to patients with unresectable colorectal hepatic metastasis.

**Methods:** This was an open-label, multi-center, single arm study, of unresectable colorectal hepatic metastasis patients who had failed standard therapy from 10/2006-10/2008. Patients received repeat embolizations with irinotecan loaded beads (max 100 mg per embolization) per treating physician’s discretion.

**Results:** Fifty-five patients underwent 99 treatments using irinotecan drug eluting beads. The median number of total treatments per patient was 2 (range of 1-5). Median length of hospital stay was 23 hours (range 23 hours - 10 days). There were 30 (30%) sessions associated with adverse reactions during or after the treatment. The median disease free and overall survival from the time of first treatment was 247 days and 343 days. Six patients (10%) were downstaged from their original disease status. Of these, four were treated with surgery and two with RFA.

Neither number of liver lesions, size of liver lesions or extent of liver replacement (<= 25% vs >25%) were predictors of overall survival. Only the presence of extrahepatic disease ($p = 0.001$), extent of prior chemotherapy (failed 1st and 2nd line vs > 2 line failure) ($P = 0.007$) were predictors of overall survival in multivariate analysis.

**Conclusions:** Chemoembolization using irinotecan loaded beads was safe and effective in the treatment of patients as demonstrated by a minimal complication rate and acceptable tumor response.

---

**REVIEW**

In 2009 Martin et al published interim results from an open-label, multi-centre, single-arm study and evaluated the role of DC Bead™ irinotecan (DEBIRI®) in the treatment of liver metastases from colorectal cancer. Fifty-five patients with confirmed diagnosis of liver-dominant metastatic colorectal cancer, liver involvement of less than 75%, preserved liver function and ECOG PS 0-2 or Karnofsky 60-100% were treated within the study.

DEBIRI® was administered in an outpatient setting, using a lobal approach with 100mg of irinotecan loaded into each DC Bead™ vial (mainly 100-300µm).

Adverse events were seen in 29% of patients. Patients who received greater than 100mg irinotecan in the first treatment only, were more likely to suffer an adverse event ($p<0.0001$).

During a median follow-up of 18 months, 12 patients died, most of them due to disease progression. One patient died of liver failure. This patient had baseline BRB of 1.9mg/dl, a liver involvement of 26-50% with total target lesion size of 12.9cm.

Tumour response was seen in 80% patients at 6 months and 54% at 12 months according to EASL. According to RECIST, 56% responded at 6 months and 40% at 12 months.

The authors conclude that DEBIRI® is safe and effective in the treatment of patients with unresectable metastatic colorectal cancer.
A further paper by Martin et al. focuses on those patients from the original 55 who were either downstaged to resection or treated in the neo-adjuvant setting. Eleven (20%) patients demonstrated either significant response and downstaging of their disease or stable disease without extra-hepatic disease progression allowing for resection, ablation or a combination of both.

All of these 11 patients had multiple liver metastases, with nine patients having less than 25% liver involvement. They all had also received systemic chemotherapy, including either FOLFOX, FOLFIRI, bevacizumab or capecitabine. Three patients were treated with concurrent irinotecan and cetuximab while on hepatic arterial therapy.

After TACE, median length of hospital stay was 23 hours. One patient suffered an adverse event of post-embolic syndrome. No peri-operative mortality was reported. One patient suffered a biloma which was resolved with percutaneous drainage and another patient experienced a minor wound infection.

Pathological evaluation showed no evidence of chemotherapy-associated steatohepatitis. Overall, pathological response in resected specimens was 90%.

Median disease-free interval was 9 months and median overall survival 12 months.

In the authors’ view, this initial evaluation confirms the activity of this therapy in the management of colorectal cancer liver metastasis. They also consider it to be an acceptable treatment option for evaluating the overall metastatic biology prior to planned hepatic resection.

...this initial evaluation confirms the activity of this therapy in the management of colorectal cancer liver metastasis. [The authors] also consider it to be an acceptable treatment option for evaluating the overall metastatic biology prior to planned hepatic resection.
DC Bead™ Chemoembolisation for the Treatment of Primary [DEBDOX®] and Secondary [DEBIRI™] Liver Cancer

### Table

<table>
<thead>
<tr>
<th>Patient</th>
<th>Prior Liver Therapy</th>
<th>Reason for Unresectability and Initial Bead Treatment</th>
<th>Number of Bead Treatments</th>
<th>Operation After Bead Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Lobectomy</td>
<td>Insufficient remnant liver</td>
<td>2</td>
<td>Ablation</td>
</tr>
<tr>
<td>2</td>
<td>Lobectomy</td>
<td>Number and location</td>
<td>2</td>
<td>Ablation</td>
</tr>
<tr>
<td>3</td>
<td>Lobectomy</td>
<td>Location</td>
<td>1</td>
<td>Ablation</td>
</tr>
<tr>
<td>4</td>
<td>Ablation</td>
<td>Location</td>
<td>2</td>
<td>Ablation + Resection</td>
</tr>
<tr>
<td>5</td>
<td>Ablation</td>
<td>Number and location</td>
<td>2</td>
<td>Ablation + Resection</td>
</tr>
<tr>
<td>6</td>
<td>Ablation</td>
<td>Number and location</td>
<td>2</td>
<td>Atypical Resection</td>
</tr>
<tr>
<td>7</td>
<td>None</td>
<td>Lung metastases</td>
<td>3</td>
<td>Lobectomy</td>
</tr>
<tr>
<td>8</td>
<td>None</td>
<td>Lung metastases</td>
<td>3</td>
<td>Atypical Resection</td>
</tr>
<tr>
<td>9</td>
<td>None</td>
<td>Lung metastases</td>
<td>3</td>
<td>Atypical Resection</td>
</tr>
<tr>
<td>10</td>
<td>None</td>
<td>Portal lymph nodes</td>
<td>3</td>
<td>Lobectomy</td>
</tr>
<tr>
<td>11</td>
<td>None</td>
<td>Portal lymph nodes</td>
<td>3</td>
<td>Lobectomy</td>
</tr>
</tbody>
</table>

Table adapted from Bower M, Metzger T, Robbins K et al, HPB (Oxford) 12 (2010): 31-36

### Conclusion

DC Bead™ has been shown to produce high response rates with a very favourable safety profile in HCC, cholangiocarcinoma, neuroendocrine metastases and colorectal metastases. Furthermore, data produced by the same authors in the treatment of colorectal cancer provide further evidence that supports the use of DC Bead™ in this indication.

Data also show that patient selection may be a key factor in ensuring optimal results. In the case of primary liver cancer, patients with advanced stages of cirrhotic and/or cancer disease were excluded from treatment. For metastatic disease, patients with high degree of extrahepatic disease, a very high liver involvement and/or liver failure were also excluded from treatment.

The evidence from these data supports the use of DC Bead™ for treatment of primary and secondary liver cancer. Owing to limited data and heterogeneity of studies for indications outside HCC, further trials are required in order to confirm these results. In the meantime and given the poor prognosis and limited efficacy of existing therapies for these malignancies, DC Bead™ should be considered as a treatment option provided the patient is a good candidate for such therapy.
有序信息:

<table>
<thead>
<tr>
<th>产品名称</th>
<th>DC Bead™</th>
<th>DC Bead™</th>
</tr>
</thead>
<tbody>
<tr>
<td>标签颜色和尺寸</td>
<td>70-150µm</td>
<td>100-300µm</td>
</tr>
<tr>
<td>Volumes of Beads</td>
<td>2ml</td>
<td>2ml</td>
</tr>
<tr>
<td>产品代码</td>
<td>DC2V001</td>
<td>DC2V103</td>
</tr>
</tbody>
</table>

重要信息

**DC Bead™指示：**
- DC Bead™是专为治疗恶性肝血管病变而设计的。
- DC Bead™是可溶于水的，可在灌注前装入。
- DC Bead™在静脉内使用。
- DC Bead™变性后，可被冲溶。
- DC Bead™对其他药物兼容。

**DC Bead™和DC Bead™的重要信息：**
- 将DC Bead™和DC Bead™应按照当地指南进行使用。
- 确保DC Bead™和DC Bead™适合所选区域。
- 确保DC Bead™和DC Bead™适合所选定的血管。

**警告：**
- 灌注后，DC Bead™和DC Bead™可能在体外混合。
- DC Bead™和DC Bead™可能附着在血管内。
- DC Bead™和DC Bead™可能在血管内被冲溶。

**潜在并发症：**
- DC Bead™和DC Bead™可能引起血管损伤。
- DC Bead™和DC Bead™可能引起血管缩小。
- DC Bead™和DC Bead™可能引起血管重构。

**注意事项：**
- DC Bead™和DC Bead™应在适当情况下使用。
- DC Bead™和DC Bead™应在适当情况下使用。
- DC Bead™和DC Bead™应在适当情况下使用。

DC Bead™和DC Bead™是Biocompatibles UK Ltd在英国的商标。DC Bead™和DC Bead™在英国是BTG International集团的商标。DC Bead™和DC Bead™在其他国家可能无法使用。

DC Bead™和DC Bead™是Biocompatibles UK Ltd的商标。DC Bead™和DC Bead™在英国是BTG International集团的商标。DC Bead™和DC Bead™在其他国家可能无法使用。

DC Bead™和DC Bead™是Biocompatibles UK Ltd的商标。DC Bead™和DC Bead™在英国是BTG International集团的商标。DC Bead™和DC Bead™在其他国家可能无法使用。

DC Bead™和DC Bead™是Biocompatibles UK Ltd的商标。DC Bead™和DC Bead™在英国是BTG International集团的商标。DC Bead™和DC Bead™在其他国家可能无法使用。