DC Bead^{M1} managing metastatic disease: Clinical rationale and pilot data

Robert Martin, MD, PhD
Associate Professor of Surgery
Director, Division of Surgical Oncology
University of Louisville School of Medicine

Louisville Collaborative BEAD Registry

www.ULBeadRegistry.com

Hepatic Arterial Therapy and Metastatic Disease to Liver

- DEBIRI and DEBDOX have been proven to be effective in Metastatic Dz to liver
- Most common bead size used in Metastatic Colorectal Cancer -100-300
- Most Common Dose is one vial w/ 100mg
- Past experience has demonstrated when, >1 vial used and/or >150mg used
  - Sig increase in SAE's

Martin et al W J Surg Onc

Rationale

- Thus if a smaller more **Precise** bead existed could this overcome the current limitations that we have?
  - i.e. Limited dosing, early stasis, pain

Rationale

- To develop a product that is best suited to treating the different pathology of metastatic disease:
  - Deliver a consistent clinically relevant dose that compliments systemic chemotherapy
  - To provide benefit in the treatment of hypovascular liver mets
  - To enable microsatellite sites to be treated

DC Bead M1

- Developed to meet the needs of a different pathology and delivery technique in metastatic disease:
  - Hypo-vascularised tumours
  - Lobar infusion and disperal
  - Ability to deliver a consistent dose (100mg irinotecan)
  - Deeper penetration of the tumour bed
  - Treatment of microsatellites not visible on angio
  - Within the current size/safety profile of DC Bead
    - Larger than 70 micron to minimise the risk of shunting
    - Larger than 40 micron to eliminate the need for MAA mapping

Product - Overview

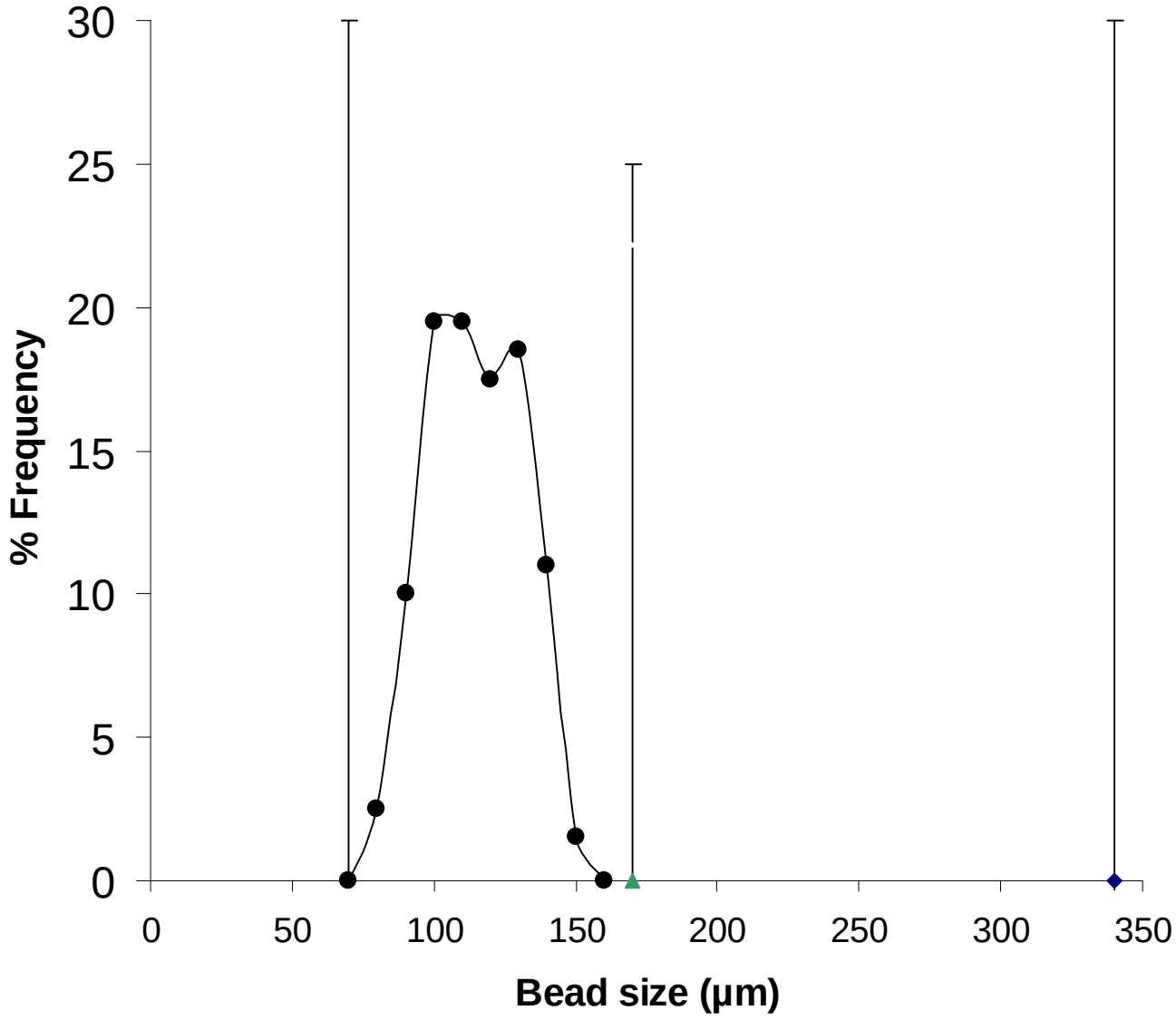
Size - 70-150 µm

2 ml DC Bead M1 in 4 ml saline

Black cap with black and yellow label

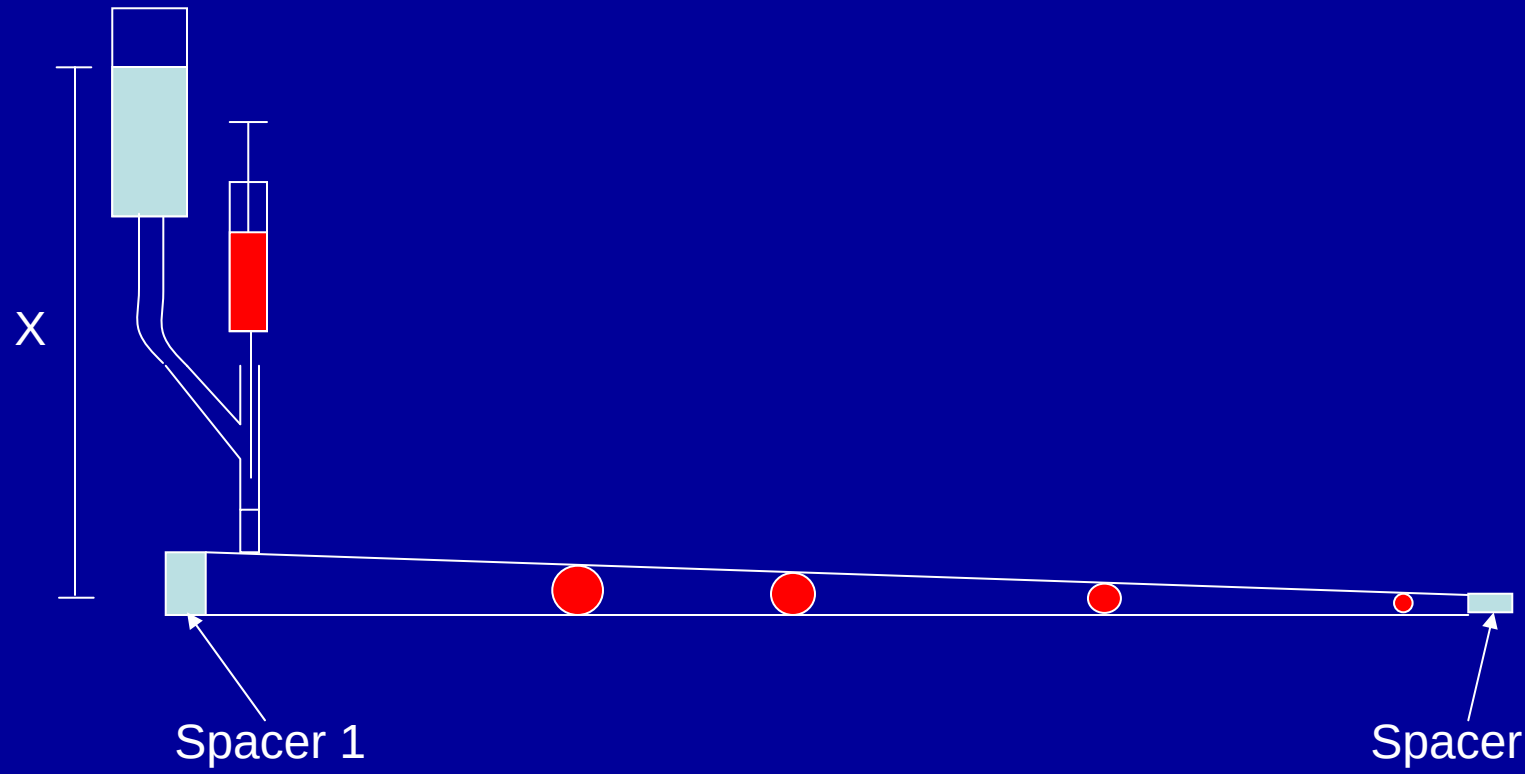
DC Bead M1 is **CE Marked** for use with **irinotecan**

DC Bead M1 distribution within known parameters



DC Bead M1 ensures beads are within the established safety profile of DC Bead

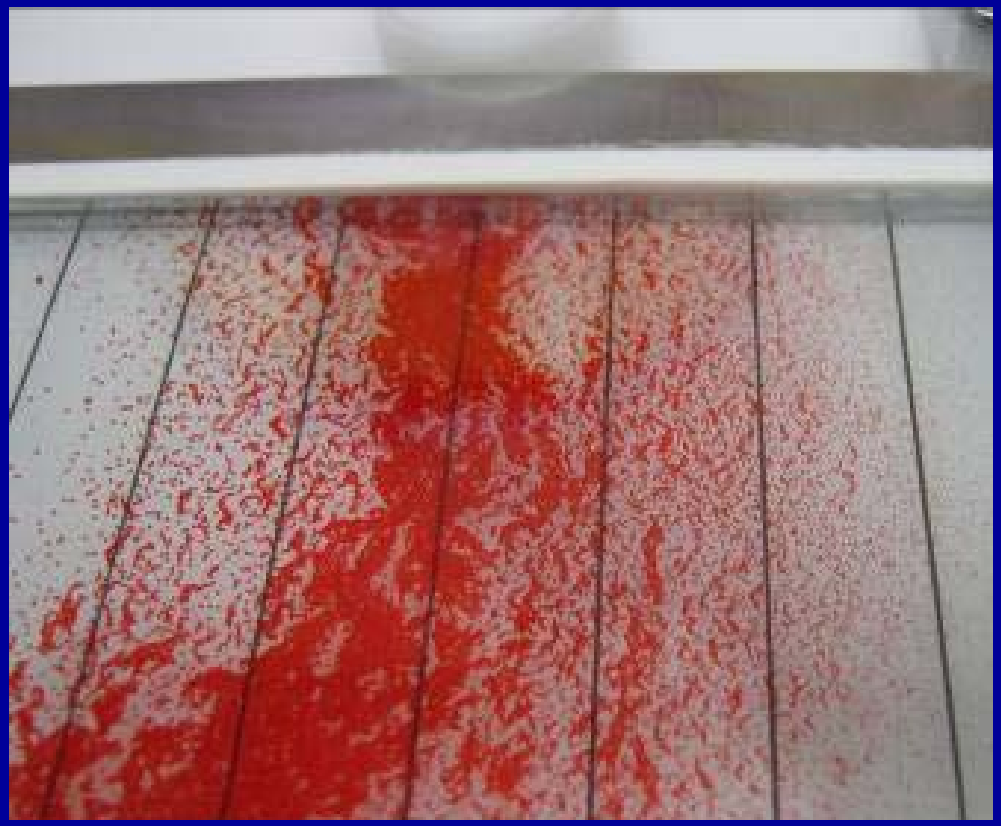
In Vitro model to visualise DC Bead M1 distribution



Courtesy of Drs Dreher, Sharma & Wood: NIH Center(USA) for interven oncology

In Vitro model to visualise DC Bead M1 distribution

DC Bead 1-300 micron

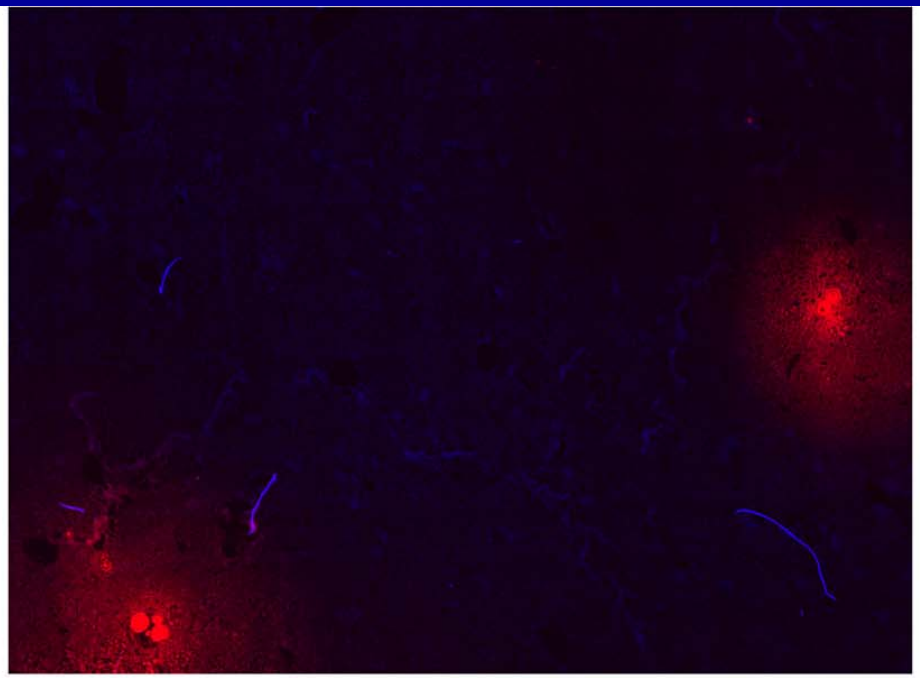


Even distribution across 100-300µm range

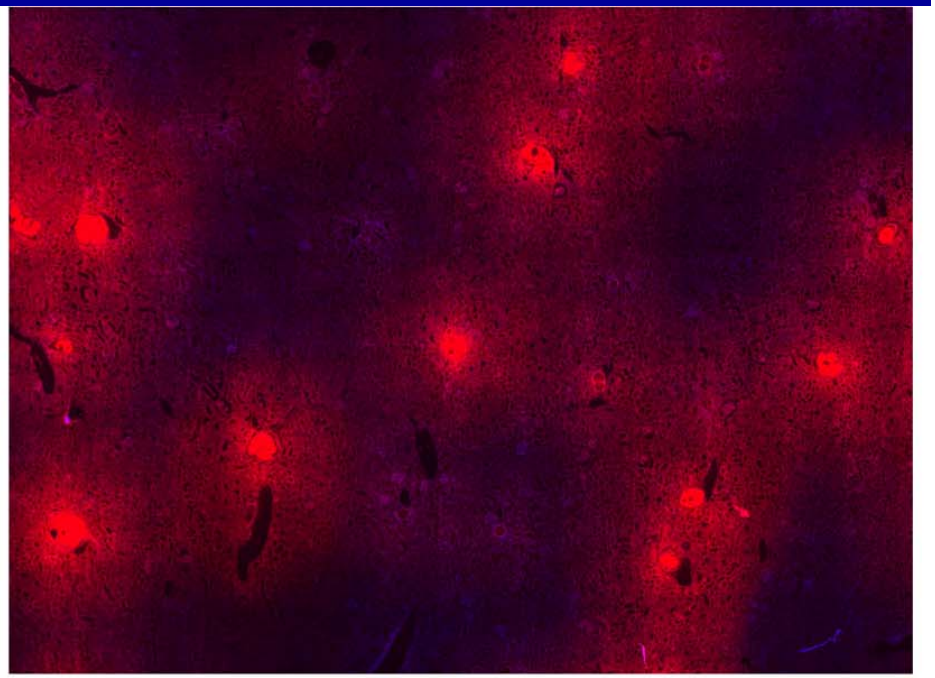
DC Bead M1

Narrow and consistent distribution

Pre-Clinical model DC Bead^{M1} distribution



100-300µm DC Bead



DC Bead ^{M1}

Pre-Clinical demonstration of deeper bead distribution with DC Bead^{M1} vs DC Bead

Courtesy of Drs Dreher, Sharma & Wood: NIH Center(USA) for interven oncology

Angiographic Endpoints

- End point:
  - The injection should be stopped once intra lesional stasis has been achieved or the whole dose has been delivered (2ml DC Bead).
  - The aim of the treatment should be to deliver the whole dose
  - No additional embolic should be used

Initial Clinical Evaluation

- 13 Patients undergone 20 M1 Bead treatments
- 11 for Met Colorectal, 1ICC, 1 Met panc
- This group was then compared to recent group (n=160 pts) undergoing 100-300 micron bead treatment

Why M1 Beads?

- Size of tumors – treating small <1.5cm diffuse miliary dz
- Vascularity – small feeding vessels
- Failed prior 100-300 micron bead
  - Defined as <75mg delivered prior

Bead Size	100-300	M1
Extent of Liver Disease Distinct # Numerous	 74% 26%	 11 (84%) 2 (16%)
Liver Involvement % <25% 26-50% >50%	 56% 36% 8%	 7 (53%) 5 (47%) 0
Number Liver tumors (median, range)	3 (1-25)	11 (1-15)
# Target Lesion(s) Size (median, range)	5 (1-5)	2.8 (1.4-6.3)
Total Sum Target Size (Median. Range)	8.4 (2.7-32.4)	6.7 (1.4-9.8)
Extrahepatic Dz	30%	1

Prior Therapy to Liver

Bead Size	100-300	M1
Prior Systemic Chemotherapy Regimens		
FOLFOX	55%	6
FOLFIRI	25%	2
Oxaliplatin	13%	0
Avastin	40%	6
Doxorubicin	1%	0
Other	42%	0
Prior Liver Surgery		
Hepatic Resection (lobectomy)	25%	4 (30%)
Ablation	27%	2 (15%)
Prior HAT		
TACE	7%	2 (15%)
Bland	0	0
Yttrium	5%	0

	N=300 total DEBIRI treatments	N=20 DEBIRI^{M1} treatments
Number of Bead	2 (range 1-5)	
1	159 (52%)	6
2	86 (28%)	7
3	35 (12%)	5
4	20	2
5	2	0
6	1	0
7	0	0
Location		
Right	61%	11 (55%)
Left	37%	9 (45%)
Middle	9%	0
Segmental	11%	0

	N=300 total DEBIRI treatments	N=20 DEBIRI^{M1} treatments
Dosages Delivered <100mg 100mg	 77% 23%	 100%
Total Hepatic Exposure Irinotecan	 100 (20-450)	 100 (100-400)
Level of Branching Lobar Segmental Sub-Segmental	 75% 19% 5%	 17 (85%) 3 0
Degree of Occlusion None Partial Near Complete	 0% 39% 26% 35%	 2 16 (80%) 2 0
LOS	23 hour (Out– 20 days)	23 hours for all
Adverse Events (%)	19%	5%

Summary

- DC Bead M1 has a unique size range and distribution
- Delivers a consistent dose that compliments systemic chemotherapy
- Allows for full dosing with out pre-mature endpoint
- Provide benefit in the treatment of hypovascular liver mets
- Enables microsatellite sites to be treated