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ORIGINAL ARTICLE

Dual-balloon infusion microcatheter for selective drug-eluting bead transarterial chemoembolization: initial feasibility study

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PURPOSE
We aimed to demonstrate feasibility of the use of a dual-balloon infusion microcatheter for segmental/subsegmental drug-eluting bead transarterial chemoembolization (DEB-TACE).

METHODS
Over a 16-month period, 15 segmental and 21 subsegmental DEB-TACE procedures were attempted using a dual-balloon anti-reflux microcatheter (IsoFlow™ microcatheter, Vascular Designs Inc.) in 21 patients (15 males; median age, 61 years; range, 49–82 years) with hepatocellular carcinoma (Barcelona clinic liver cancer stage A [n=4]; B [n=12]; C [n=5]) with one to three tumors, median size of 3.4 cm (1.2–9 cm). Follow-up enhanced computed tomography or magnetic resonance imaging was obtained at one month then subsequently every three months for one year. Technical success was evaluated. Modified RECIST criteria was used for target tumor response assessment. Safety was evaluated by assessing for arterial injury and hepatic injury at the time of the procedure and subsequent evidence of complications and liver toxicity.

RESULTS
In 26 of the procedures, the segmental/subsegmental arteries were thought not to be easily selected with standard microcatheters due to the arterial branches being severely tortuous/angulated or atretic from prior TACE or anti-angiogenic therapy or could not be catheterized. Radiologic response assessment of treated tumors demonstrated 32% complete response, 19% partial response, 34% stable disease, and 15% progressive disease. No complications occurred. The median time to progression for the targeted tumors was 7 months (range, 3–12 months).

CONCLUSION
DEB-TACE, using this dual-balloon anti-reflux infusion microcatheter is feasible and safe.

It has been recommended that drug-eluting bead transarterial chemoembolization (DEB-TACE) be performed in segmental or subsegmental selective fashion whenever possible (1). Selective treatment spares non-tumor containing liver and might reduce hepatic toxicity. Furthermore, non-tumor supplying hepatic arterial vasculature is spared from embolic effects such that they may be catheterized if subsequent catheter directed therapy is required for new tumors arising in the previously treated vascular distributions (2–4).

Advancements in microcatheter and guidewire technology have facilitated the performance of segmental/subsegmental arterial catheterization. However, in some cases selective catheterization remains challenging or not possible. This may be due to an acute angulation at the origin of the vessel, particularly in cirrhotic livers, or when the vessel is diminutive/atretic as may result from prior TACE or anti-angiogenic therapy. In response to these challenges, novel techniques and catheter modifications have been developed, including controlled isolation of a single arterial branch during therapy (5–7).

The IsoFlow™, dual-balloon, anti-reflux infusion catheter (Vascular Designs) is an FDA approved microcatheter (Fig. 1). The design of this catheter allows isolation of target, tumor-supplying arteries between two compliant balloons. As a result, an isolated lateral infusion of chemoembolic agent can be performed, without reflux and with maintained perfusion of vasculature distal to the catheter. The purpose of this study was to describe the initial use of this dual-balloon infusion microcatheter, providing the initial evaluation of feasibility, safety,

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and technical success of its use for DEB-TACE of hepatocellular carcinoma (HCC).

Methods

Patient selection

This retrospective review study was approved by the hospitals' institutional review boards, with waiver of informed consent. Inclusion criteria for DEB-TACE included: HCC proven by histology or according to AASLD criteria (8), tumors not felt to be amenable to operable resection or ablation (due to patient comorbidities, tumor size, proximity to adjacent organs/vessels, or portal hypertension), one to four measurable tumors on contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI), and preserved liver function (Child Pugh A–B7). Exclusion criteria included Child Pugh stage B8-C, ECOG status >2, total bilirubin ≥3 mg/dL, hepatic encephalopathy, portal vein occlusion, and contraindication to angiography (9). The decision to perform DEB-TACE was made at the institutional multidisciplinary conference. Hepatic lobar and segmental arterial supply to the target tumor was evaluated on axial and coronal reconstructed images from the arterial phase of the contrast-enhanced CT or MRI, obtained within one month of treatment. Initial determination of hepatic and tumor supplying arterial diameter and tortuosity was made. Target segmental/subsegmental arterial branches were thought to be "atretic" if they appeared whisp like, difficult to visualize or with suggestion that they might have a diameter smaller than the 2.8 French (F) microcatheter, when assessing tumor supplying vascularity on cross-sectional imaging and during angiography.

Equipment and procedures

The procedures were performed under moderate sedation using midazolam and fentanyl. Femoral arterial access was achieved and a 5 F sheath placed. Diagnostic angiography of the superior mesenteric artery and celiac trunk was first performed with a 4 or 5 F Simons 1 or Cobra C2 angiographic catheter (Boston Scientific). When treating the first five tumors in three patients, the target segmental/subsegmental arteries could be easily catheterized with standard microcatheters. In these initial cases the standard microcatheter was then removed and exchanged for the IsoFlow catheter, to be used for DEB-TACE infusion, demonstrating the initial proof of principle (Fig. 2). In all other cases, the decision to use the IsoFlow dual-balloon anti-reflux infusion microcatheter to isolate tumor supplying vascularity was made if: 1) it was thought that the targeted segmental/subsegmental artery could not be easily catheterized, based on review of initial pretreatment cross-sectional imaging and/or celiac /superior mesenteric artery (SMA) angiography, or 2) initial, unsuccessful attempt to catheterize the tumor supplying segmental/subsegmental artery using the institutions' usual microcatheters (Prowler Plus, Cordis or Merit Maestro, Merit Medical), or 3) attempt was being made to avoid delivery of chemoembolic to adjacent liver, when hepatic function was marginal (total bilirubin >2.5 or Child Pugh Class B7).

IsoFlow catheter use

The IsoFlow catheter is 150 cm long with a proximal and distal outer diameter of 3.5 F and 2.3 F, respectively. Near the distal end of the catheter are two compliant balloons, indicated by radiopaque marker bands, which can be inflated from 2 to 6 mm (Fig. 1). These balloons are positioned proximal and distal to a 10 mm long infusion segment containing multiple side holes. This infusion catheter contains three lumens: one for inflation of the balloons, a second for infusion through the side holes in the inter-balloon segment, and a third to accommodate a 0.014-inch guidewire. The infusion side holes allow delivery of embolics measuring up to 300 µm. The guidewire lumen has a side hole proximal to the balloons that communicates with the vessel lumen. When the wire tip is sufficiently retracted, the side hole communicates with the end hole through the guidewire lumen, allowing blood flow from a proximal to distal location downstream from the occlusion balloons. Using an 0.014-inch wire, the IsoFlow™ catheter is inserted coaxially, through a 5 F guiding catheter, with a 0.056-inch inner diameter (Cordis) positioned within the ostium of the celiac axis or SMA.

Two attending interventional radiologists with 5 and 12 years of experience and one fellow used this dual-balloon infusion catheter for selective DEB-TACE of one to three tumors, at each treatment session. The IsoFlow catheter was positioned to isolate the segmental or subsegmental tumor supplying vascularity. One vial of 100–300 µm LC Bead® (BTG International Inc.) containing 50 mg doxorubicin and mixed with 10 mL Visipaque 320 (Iodixanol, GE Healthcare) was administered. The balloons were deflated and contrast administered after each mL of the chemoembolic infused. Dose infusion was terminated if reflux or stasis was seen when the balloons were deflated or if there was staining of portal branches near the tumor, during infusion. Immediately following DEB-TACE, an unenhanced cone-beam CT was performed to assess for contrast/DEB-TACE

Main points

- The dual-balloon infusion microcatheter allows isolated DEB-TACE infusion of segmental/subsegmental tumor supplying arteries, allowing treatment of tumors which otherwise might be difficult to selectively catheterize.
- The catheter prevents reflux, minimizing non-target delivery while maintaining perfusion of the downstream parent artery.
- The use of the catheter is feasible, with about 90% technical success rate, and safe, with acceptable rates of tumor response.

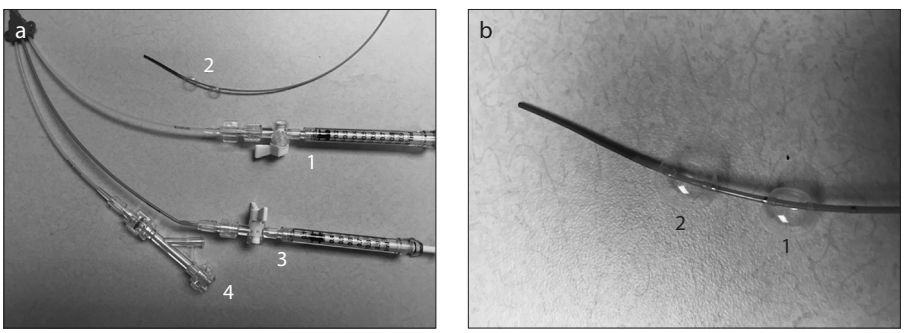

Figure 1. a, b. IsoFlow catheter design. Panel **(a)** shows the overview of design. The chemoembolic agent is infused through the upper port syringe (1), exiting outflow channels between the two occlusion balloons (2), to be delivered to vessels arising perpendicular from the catheterized vessel. The middle port inflates and deflates the occlusion balloons (3). The lower port, with rotating hemostatic valve, accommodates the 0.014-inch guidewire (4). Contrast can also be infused via the lower port into vessels distal to the occlusion balloons. Panel **(b)** shows magnified view of occlusion balloons proximal (1) and distal (2) to the outflow channels.

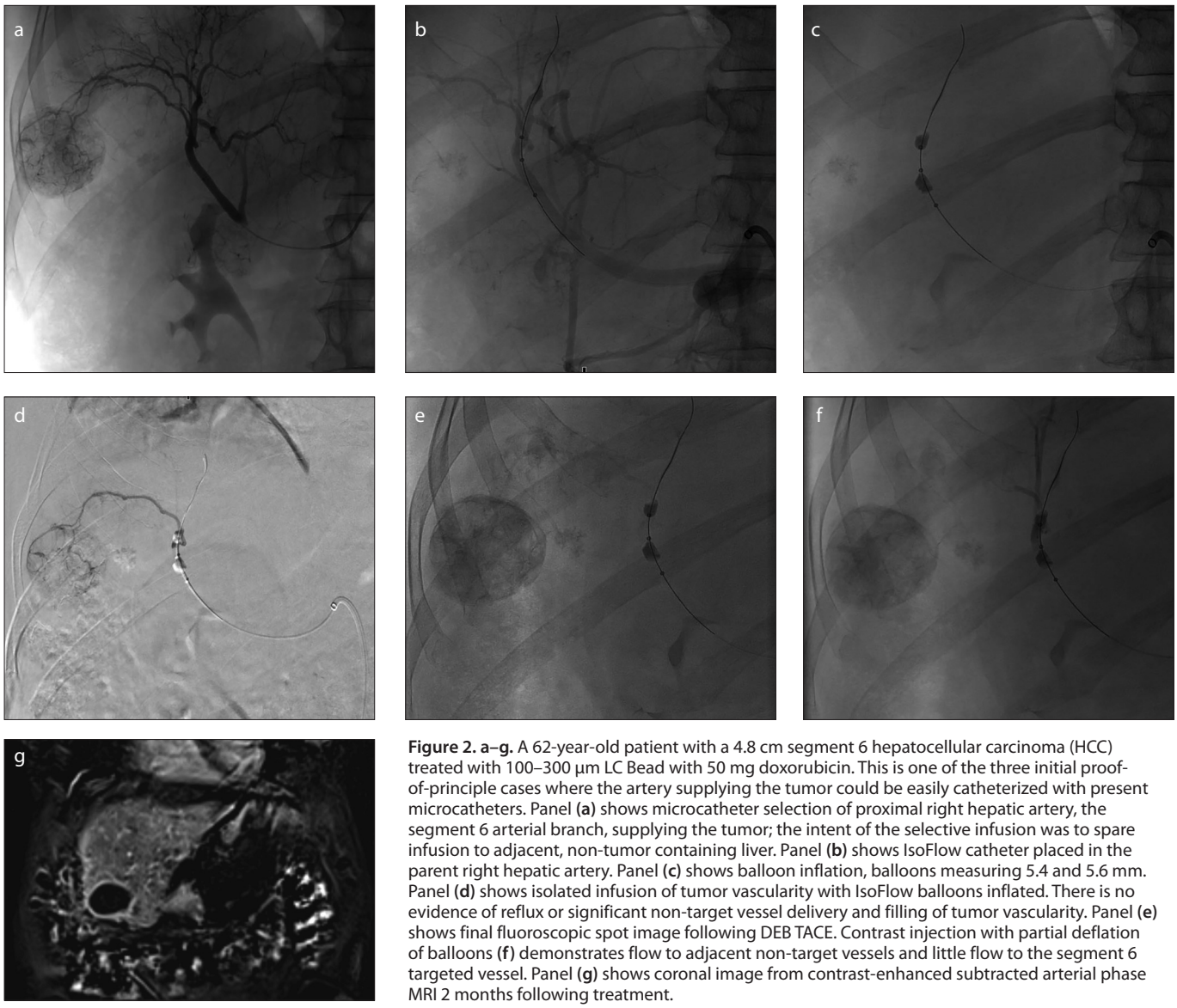

Figure 2. a–g. A 62-year-old patient with a 4.8 cm segment 6 hepatocellular carcinoma (HCC) treated with 100–300 µm LC Bead with 50 mg doxorubicin. This is one of the three initial proof-of-principle cases where the artery supplying the tumor could be easily catheterized with present microcatheters. Panel **(a)** shows microcatheter selection of proximal right hepatic artery, the segment 6 arterial branch, supplying the tumor; the intent of the selective infusion was to spare infusion to adjacent, non-tumor containing liver. Panel **(b)** shows IsoFlow catheter placed in the parent right hepatic artery. Panel **(c)** shows balloon inflation, balloons measuring 5.4 and 5.6 mm. Panel **(d)** shows isolated infusion of tumor vascularity with IsoFlow balloons inflated. There is no evidence of reflux or significant non-target vessel delivery and filling of tumor vascularity. Panel **(e)** shows final fluoroscopic spot image following DEB TACE. Contrast injection with partial deflation of balloons **(f)** demonstrates flow to adjacent non-target vessels and little flow to the segment 6 targeted vessel. Panel **(g)** shows coronal image from contrast-enhanced subtracted arterial phase MRI 2 months following treatment.

distribution (Alura, Philips) (10). Technical success was defined as the ability to position the dual-balloon anti-reflux microcatheter to treat the target tumor and achieve stasis or near stasis in the supplying subsegmental or segmental arteries, demonstrated when the balloons are intermittently deflated following every mL infused, without angiographic demonstration of reflux during DEB-TACE infusion.

Clinical and imaging follow-up

During this pilot study, follow-up clinic appointment and imaging (multiphase CT or MRI) was performed at 1 month and 3, 6, 9, and 12 months after TACE. Radiologic tumor response, based on contrast-enhanced MRI or CT, was assessed by measuring the treated tumors and categorizing the percent change in tumor enhancement into four categories (complete response, partial response, stable disease, disease progression) as defined by modified RECIST criteria (11, 12). Treatment was repeated if follow-up imaging demonstrated persistent enhancing tumor and the patient continued to meet inclusion criteria. The safety of the procedure was evaluated by assessing for symptoms and imaging findings suggestive of vascular injury, biliary ischemic injury/necrosis, abscess formation, or tumor rupture at the time of the chemoembolization and during subsequent clinic and imaging follow-up.

Treatment-related toxicity

Baseline laboratory testing was obtained within 1 week prior to treatment. All patients underwent laboratory follow-up 1 month after treatment then every 3 months thereafter (up to 1 year). Clinically relevant toxicity, including hepatic insufficiency, was categorized in accordance with the National Institute of Health common terminology criteria for adverse events (CTCAE version 4) definitions, by assessing post-treatment serum bilirubin, albumin, leukocyte count, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels (13). In patients with liver dysfunction at baseline, toxicity was only counted if laboratory values worsened during the follow-up period.

Results

Over a 16 month period, segmental/subsegmental TACE was attempted in 21 patients (15 males; median age, 61 years;

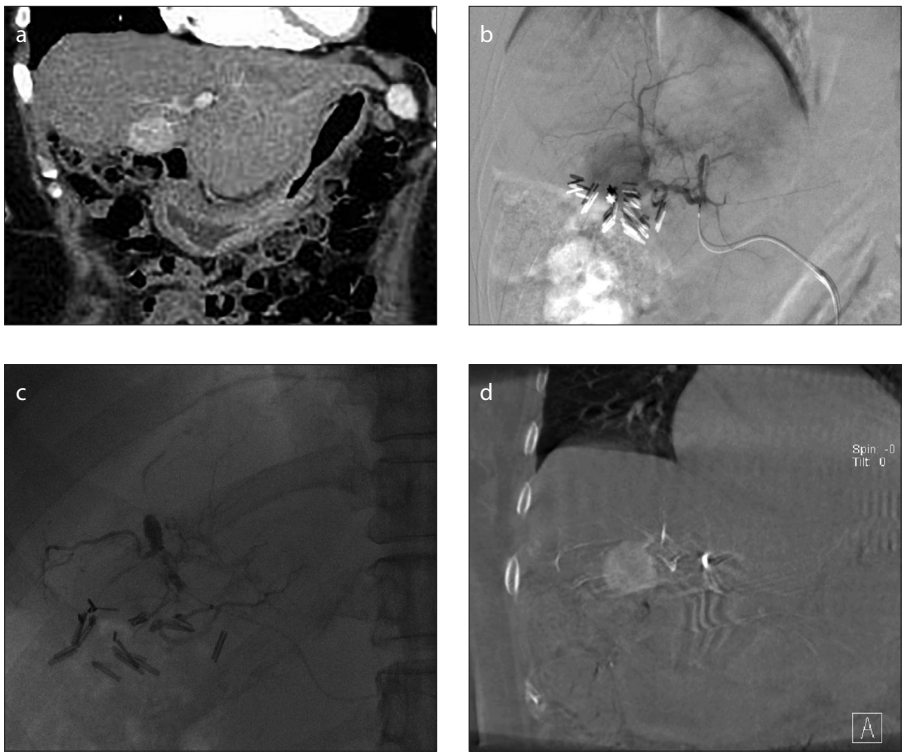

Figure 3. a–d. A 59-year-old patient with 3.9 cm segment 6 HCC treated with 100–300 µm LC Bead with 50 mg doxorubicin. Panel **(a)** shows coronal reconstructed image from arterial phase CT. Prowler plus microcatheter angiography of right hepatic artery **(b)** demonstrates multiple atretic central segmental vessels supplying the tumor. Panel **(c)** shows IsoFlow selection of proximal right hepatic artery. IsoFlow catheter balloon inflation, with balloons measuring 5.4 and 5.6 mm, allow isolated infusion of tumor vascularity with IsoFlow. There is no evidence of reflux or significant non-target vessel delivery. Panel **(d)** shows cone beam CT immediately following DEB-TACE.

Table 1. Baseline patient characteristics, health status, and tumor burden

Characteristic	
Patients, n	21
Age (years), median (range)	36 (49–82)
Gender (male/female), n	15/6
Health status	
Prior TACEs (2/1)	9/11
Bilobar disease (no/yes)	17/4
Child-Pugh classification (A/B)	16/5
ECOG performance status (0/1)	14/7
Tumor burden, n of treated tumors	32
Tumors treated per patient, median (range)	2 (1–3)
Treated tumor size (cm), median (range)	3.4 (1.2–9)
BCLC stage (A/B/C)	4/12/5

TACE, transarterial chemoembolization; ECOG, Eastern cooperative oncology group; BCLC, Barcelona clinic liver cancer scale.

range, 49–82 years) with HCC. Patients were diagnosed with Barcelona clinic liver cancer (BCLC) A (n=4), BCLC B (n=12), and BCLC C (n=5), and harbored 1–3 tumors, for a total of 36 target lesions. Median tumor size was 3.4 cm (range, 1.2–9 cm) (Tables 1, 2). Twenty of these patients had prior DEB-TACE and all had cirrhosis (Tables 1, 2), perhaps contributing to the target tumor supplying arteries being atretic and/or tortuous. In nine patients, attempts were made to treat a single tumor. In nine patients, two tumors were treated in a single session by deflating the balloons and repositioning the catheter in another target vessel. In three patients, attempts were made to treat three tumors in a single treatment session.

In six patients, review of prior cross-sectional imaging suggested atretic diminutive diameter of the segmental/subsegmental arterial supply to the tumor or severe angulation at the origin of the vasculature supplying the tumor. In these six plus five additional patients initial celiac, or SMA angiography with replaced right hepatic arteries, demonstrated atretic branches or severe angulation at the origin of the target branch. In five patients, initial attempts to catheterize target subsegmental or segmental arterial branches with the standard microcatheters were unsuccessful (Fig. 3). In five patients, this dual-balloon microcatheter was also used to avoid delivery of chemoembolic to adjacent liver, when hepatic function was marginal (total bilirubin >2.5 or Child Pugh Class B7).

The technical success rate was 89%. In two patients (total of four tumors), the catheter did not track to the target subsegmental arteries supplying the tumors and thus could not be used (Table 2, "not advance"). In general, tracking was significantly improved when saline was infused through the guide catheter via a Tuohy Borst rotating hemostatic valve. Reflux was noted in one case were the occlusion balloons did not appear to approximate the right hepatic artery walls at the origin of the middle hepatic artery. In one case, the catheter became occluded during infusion, which was cleared with further flushing once removed from the patient, and reinserted. The catheter was advanced to the segmental arteries to treat 15 tumors and to the subsegmental branches in attempt to treat 21 tumors.

The DEB is infused with the syringe and is not dependent on forward blood flow during infusion. The DEB/contrast clears from the segmental/subsegmental vasculature, when being infused and when balloons were deflated. No filling of intrahepatic collateral arteries supplying other segments of the liver was evident during infusion. One hundred percent of the intended dose, one vial DEB containing 50 mg doxorubicin, was delivered in 78% of the cases. In 22% of the cases infusion was discontinued when there was staining of portal branches near the tumor or non-clearing of the contrast/LC Bead column when the balloons were deflated.

Table 2. Target tumor characteristics and response

Case#	Size (cm)	Selection	BCLC	Response at 3 months	TTP (months)	Prior TACEs
1	1.2, 2.1	Segmental	A	CR/PR	NA/6[a]	1
2	5.9	Segmental	B	CR	NA	1
3	7, 5.3	Segmental	C	PR/PR	5/8	2
4	3.6, 1.5	Segmental	B	PR/SD	4/NA	2
5	3.4, 1.2	Subsegmental	B	SD/CR	9/NA	2
6	9	Segmental	C	PD	6[b]	2
7	2.3, 3, 2	Subsegmental	A	SD/SD/CR	NA/9/NA	1
8	2.7, 3	Subsegmental	A	PD/SD	12	2
9	7.9	Segmental	B	SD	6	2
10	3.5, 1.5	Subsegmental	B	DP/CR	4/NA	1
11	4.2	Segmental	A	SD	NA	1
12	1.4, 5	Segmental	C	SD/SD	9/6	1
13	1.8, 1.8	Subsegmental	B	CR/CR	NA/NA	1
14[c]	3.5, 2.5	Subsegmental	B	CR/PR	9/12	2
15	4.2	Subsegmental	B	Not advance[d]		0
16	3.6	Segmental	B	PD	3[b]	1
17	1.5, 1.5, 7.6	Subsegmental	C	SD/SD/PD	10/NA/3	2
18	4.2, 2.1, 2.2	Subsegmental	B	Not advance[d]		2
19	8.3	Segmental	B	CR	9	1
20	3.7	Subsegmental	B	CR	NA	1
21	4.8	Segmental	C	PR	3	1

BCLC, Barcelona clinic liver cancer scale; TTP, time to tumor progression in months; TACE, transarterial chemoembolization; CR, complete response; PR, partial response; NA, no target tumor progression during the one year follow up period; SD, stable disease; PD, progressive disease.
[a]Lost to follow-up within one year of DEB-TACE; [b]Expired within one year of DEB-TACE; [c]Occluded catheter; [d]Catheter did not track to the target subsegmental arteries supplying the tumors.

Table 3. Summary of mRECIST response rates for treated tumors, 3 months following IsoFlow-assisted DEB-TACE

	Tumors, n (%)
Complete response	10 (32)
Partial response	6 (19)
Stable disease	11 (34)
Progressive disease	5 (15)

mRECIST, modified Response Evaluation Criteria in Solid Tumors; DEB-TACE, drug-eluting bead transarterial chemoembolization.

At the 3-month imaging follow-up, complete response was demonstrated in 32% of the treated target tumors and objective (complete + partial) response was demonstrated in 51% of the tumors (Tables 2, 3). Response and time-to-progression (TTP), for each tumor treated, is listed in Table 2. The median TTP for the 19 selectively treated tumors that progressed within 1 year of treatment was 7 months (range, 3–12 months) (Table 2). Eight tumors with complete response and 4 tumors with stable disease at 3 months did not progress within the 1-year follow-up period (NA in Table 2). Four tumors could not be treated using the catheter and so are not included in assessment of response or TTP (Table 2). Treatment was repeated at the time follow-up imaging demonstrating persistent enhancing tumor partial response or progressive disease if the patient was felt to be a candidate for additional liver directed therapy, based on a review at the multidisciplinary liver tumor conference. If there was partial response and the tumor shrunk, percutaneous or laparoscopic ablation was favored provided that there were ≤3 tumors of <3 cm in size and not within 2 cm of large vessels or vital structures. In general, Y90 was favored when treatment was repeated. In case of progressive disease with multiple tumors, lobar Y90 or TACE was performed.

Postembolization angiography performed through the guide catheter following removal of the IsoFlow catheter demonstrated no evidence of IsoFlow catheter-related vessel injury, pseudoaneurysm, or dissection. In one case, during subsegmental treatment, there was spasm at the guide catheter tip which resolved with 100 µg intraarterial nitroglycerine. There were no cases of hepatic failure, biliary ischemic injury/necrosis, abscess formation, or tumor rupture. Baseline pretreatment toxicities at 1 and 3 months following treatment are summarized in Table 4. Two patients had grade 2 leukopenia and one patient had grade 2 hypoalbuminemia and transaminase elevation at 1-month follow-up. One patient had transient grade 3 elevation of bilirubin or transaminases, within a month of treatment.

Discussion

This feasibility study demonstrates initial use of a catheter designed to allow selective DEB-TACE in cases were the segmental/subsegmental tumor supplying arterial branch may be difficult or even not possible to directly catheterize with current microcatheters. This microcatheter was indicated for use in treatment of tumors supplied by tortuous, diminutive vessels and even web-like atretic vessels such as arteries following multiple rounds of prior TACE or in severely cirrhotic livers. The dual-balloon anti-reflux microcatheter can be placed in the adjacent parent artery (e.g., right hepatic artery) and the chemoembolic infused laterally, into the perpendicular branch, such that the usual superselective segmental or subsegmental catheterization is not needed. Furthermore, the approach can prevent reflux and non-target delivery of chemoembolic agents to adjacent hepatic parenchyma, cystic artery, gastroduodenal and gastric arteries, which can result in potential complications (14, 15). In addition, non-targeted vasculature may be spared the effects of TACE which may eventually result in vascular atresia, making future treatments more challenging (16–19).

Table 4. Liver toxicities by CTCAE category

	Baseline, %	1 month, %	3 months, %
Hypoalbuminemia			
None or grade 1 (>3.0 g/dL)	95	95	95
Grade 2 (2.0–2.9 g/dL)	5	5	5
Grade 3 (0.1–1.9 g/dL)	-	-	-
Hyperbilirubinemia			
None or grade 1 (<1.9 g/dL)	85	95	100
Grade 2 (2.0–3.9 g/dL)	5	-	-
Grade 3 (4.0–13.0 g/dL)	10	5	-
Aspartate aminotransferase (AST)			
None or grade 1 (<120 U/L)	90	90	95
Grade 2 (120–200 U/L)	-	5	5
Grade 3 (200–800 U/L)	10	5	-
Alanine aminotransferase (ALT)			
None or grade 1 (<144 U/L)	80	95	95
Grade 2 (144–240 U/L)	10	5	5
Grade 3 (241–960 U/L)	10	-	-
Leukopenia			
None or grade 1 (>3000 cells/mL)	100	90	100
Grade 2 (2000–3000 cells/mL)	-	10	-
Grade 3 (1000–2000 cells/mL)	-	-	-

CTCAE, common terminology criteria for adverse events.

The capability of the dual-balloon microcatheter to selectively infuse an isolated vessel was first established treating 5 tumors, with non-tortuous parent vessels, that could easily be catheterized with usual microcatheters, as initial proof of principle, followed by use for vessels thought not to be easily catheterized. There is a short learning curve when using this catheter, placing the occlusion balloons to isolate the perpendicular vessel and laterally infusing rather than directly catheterizing the target vessel, since this approach differs from what an operator would be used to doing. It is a user dependent decision as to how long one would want to initially try usual microcatheter/wire combinations before resorting to this dual-balloon catheter. In approximately 50% of these cases, the cross-sectional imaging and initial celiac or SMA angiography would suggest difficulty for selective catheterization such as when atretic or severely tortuous arteries supply the tumor. In these cases, the dual-balloon infusion catheter was initially used.

A number of studies have described effective use of "balloon-occluded TACE" (B-TACE) for conventional lipiodol based TACE since 2013 (20, 21). This approach results in changes in intraarterial and intravenous pressures to increase drug uptake. The surefire anti-reflux catheter has also been demonstrated to change these pressure gradients when used with radioembolization and conventional TACE (22). These prior studies have demonstrated improved delivery of the chemoembolic agent. The principle mechanism of the IsoFlow balloon catheter is different. It is not known if the described pressure changes occur during use of the IsoFlow dual-balloon catheter since pressure changes were not measured as part of this study. This initial study is meant to demonstrate feasibility, safety, and technical success in a small number of patients.

Another approach to superselective delivery to vessels that cannot be catheterized is to inflate an occlusion balloon distal to the vessel being treated to direct the chemoembolic infusion to the tumor vessel using a parallel microcatheter positioned proximal to the vessel origin (6). Compared with this approach, a possible advantage of the dual-balloon anti-reflux microcatheter, described here, is that there is less chance of reflux to non-target vessels. Furthermore, the approach described here allows preserved blood flow in the parent vessel distal to the balloons used to isolate vessels arising perpendicular to the parent vessel. This is suggested by the rapid flow of contrast injected from the guide catheter entering the vessel distal to the occlusion balloons by virtue of this bypass of flow. This is a theoretical advantage and it has never been established that temporary occlusion of vasculature supplying the adjacent non-tumor containing liver is detrimental.

A limitation of the current design of the catheter is that the length of the infusion site between the two balloons is fixed at 10 mm. As a result, if adjacent vessels supplying non-tumor containing liver are within 10 mm of the tumor vessels, non-intended delivery of the DEB to these vessels would occur. Another limitation is that the balloon diameter is 2–6 mm and so can only be used in vessels of that size. Trackability of the dual-balloon catheter is an important concept when considering potential clinical applications. In two patients, the catheter would not track to the target subsegmental arteries supplying the tumors and thus could not be used. In these cases, the celiac axis and common hepatic arteries were quite tortuous. To keep vein open, low rate saline infusion through the guidewire port greatly improved overall trackability.

The complete response of 32% and objective response of 51% is similar to the 27% complete response and 52% objective response rates demonstrated with DEB TACE in the PRECISION V study (23). Other studies may report higher response rates for segmental TACE (24). An important distinction from other studies, all using standard microcatheters, is that the segmental/subsegmental vessels supplying the majority of the tumors in this study were atretic or severely tortuous making selective catheterization with standard microcatheters difficult or even otherwise not possible. This may represent a narrow clinical application. However, the IsoFlow catheter can also be used to help avoid reflux and spare adjacent liver vasculature from non-target chemoembolization in patients with usual vasculature. While designed for the indications described, the catheter can be used for any tumor supplying vasculature in place of usual microcatheters. It is speculative; however, the ability to isolate tumor supplying vasculature while avoiding infusion to adjacent vasculature might be use-

ful for treating extrahepatic malignancies such as pancreatic cancer.

This feasibility case series has limitations in that it is a retrospective review of a small number of patients. There is selection bias since the majority of the tumors could not be treated with conventional microcatheters. With this study, it cannot be proven that this delivery approach, allowing more isolated infusion without reflux, results in clear therapeutic benefits. A prospective study with randomization to IsoFlow catheter versus conventional microcatheter would be required for further evaluation of safety and clinical efficacy. However, given the similarity of response in this study versus historical data (23), and the low complication rate during DEB-TACE and IsoFlow assisted DEB-TACE, a large number of subjects would be required to have statistical significance.

In conclusion, this series demonstrates the feasibility of using the IsoFlow microcatheter for performing DEB-TACE to isolated segmental and subsegmental arteries which could not be easily catheterized using currently available microcatheters.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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