Cardiovasc Intervent Radiol (2019) 42:1322–1328
https://doi.org/10.1007/s00270-019-02232-7

CLINICAL INVESTIGATION INTERVENTIONAL ONCOLOGY

Current Trends in the Treatment of Hepatocellular Carcinoma with Transarterial Embolization: Variability in Technical Aspects

Paul Craig[1] · **Shamar Young**[1] · **Jafar Golzarian**[1]

Received: 5 February 2019 / Accepted: 22 April 2019 / Published online: 13 May 2019

Abstract
Purpose While transarterial chemoembolization (TACE) is a mainstay of treatment for unresectable hepatocellular carcinomas (HCCs), technical aspects have varied considerably in the literature. These variations lead to heterogeneity and make meaningful comparisons between articles difficult. The goal of this survey was to report international embolization practices for the treatment of HCC in an effort to understand current treatment strategies as a first step toward technique standardization.
Materials and Methods An anonymous 18 question online survey, evaluating technical aspects of TACE, was distributed via e-mail to practicing members of the five largest interventional radiology societies in Chinese and English. A total of 1160 responses were obtained from 62 countries.
Results Between regions, there were significant statistical differences in nearly all responses, including the amount of ethiodol oil used for cTACE ($p = < 0.001$). Practitioners most commonly used greater than 7.5 ml of ethiodol oil (240/506, 47.4%) and most did not utilize a specific mixing method (249/505, 49.3%). Particles utilized varied by geographical region ($p = < 0.001$), spherical embolic particles were slightly favored (363/757, 47.9%), followed closely by gelatin-based or sponge particles (279/680, 36.8%). Gelfoam was used almost exclusively in Japan and Korea (79/82 responses). LC/DC beads were the most commonly used drug-eluting bead (DEB) (450/742, 60.6%), with the most common size of DEB being 100–300 µm (354/690, 51.3%, $p = 0.07$).
Conclusion Technical aspects of transarterial embolization for HCC vary significantly by geographical location.

Keywords Chemoembolization · Hepatocellular carcinoma (HCC) · Survey

Abbreviations

CIRSE	Cardiovascular and Interventional Radiology Society of Europe
CSIR	Chinese Society of Interventional Radiology
cTACE	Conventional transarterial chemoembolization
DEB-TACE	Drug-eluting bead transarterial chemoembolization
HCC	Hepatocellular carcinoma
JSIR	Japanese Society of Interventional Radiology
KSIR	Korean Society of Interventional Radiology
TACE	Transarterial chemoembolization
TAE	Transarterial embolization
SIR	Society of Interventional Radiology

Introduction

Hepatocellular carcinoma (HCC) is a prevalent malignancy representing the third most common cause of cancer-related death worldwide [1]. Nearly 40 years ago, transarterial embolization (TAE) and classical transarterial chemoembolization (cTACE) were introduced as

✉ Paul Craig
craig278@umn.edu

[1] University of Minnesota, 420 Delaware Street SE, Minneapolis, MN 55455, USA

interventional methods in the treatment of unresectable HCC. Drug-eluting beads (DEB) TACE followed in the early twenty-first century [2–4]. To date, chemoembolization remains a mainstay of treatment for unresectable HCC, with well-documented survival benefits. However, many technical aspects of the procedure vary widely among published data and trials. One aspect that leads to this heterogeneity is that TACE is often utilized as an umbrella term to refer to three distinct, but related, procedures TAE, cTACE, and DEB-TACE.

TAE, cTACE, and DEB-TACE all utilize selective catheterization of the hepatic artery branch feeding the tumor. However, after the selection of the target hepatic artery TAE, cTACE, and DEB-TACE begin to vary. In contrast to cTACE and DEB-TACE, TAE only utilizes an embolic agent. In cTACE, cytotoxic agents mixed with ethiodol oil (Lipiodol; Guerbet, Villepinte, France) are injected; this emulsion functions as a vector to carry the cytotoxic agent(s) to the hepatic sinusoids, where the drug is gradually released from the unstable mixture [5]. This is followed by particle embolization. In DEB-TACE, chemotherapy is loaded into beads and added to water-soluble contrast. The DEBs act both as a vector for drug delivery and embolic agent to block the artery blood supply of the tumor.

Furthermore, even among published trials for each of these related treatments (TAE, cTACE, and DEB-TACE) numerous technical variations exist. For example, even within the published technical recommendations from experts, no specific drug regimen is suggested [6]. Due to the rampant heterogeneity in the technical aspects of this procedure and its follow-up methodology, it is difficult to compare various studies reported by different investigators. This limits the utility of meta-analyses and creates difficulty and frustration in comparing TA(C)E to other locoregional and systemic HCC therapies. While it will take well designed, homogenous randomized controlled trials to determine the optimal techniques for the TA(C)E procedure, an important first step is to understand the current practices, in various geographical areas around the world. Unfortunately, there is a paucity of this type of data in the literature, which is currently limited to a single country or interventional society [7–9].

The purpose of this survey, which was distributed to the largest interventional radiology societies around the world, was to determine inherent variability of TA(C)E procedures for the treatment of HCC. The less specific portion of collected data was published separately [10]; reserving the more technical aspects to be reported here.

Materials and Methods

An 18 question survey (Appendix) was created by two interventional radiologists with extensive knowledge and experience in oncology therapy and distributed through Survey Monkey and Qualtrics to members of the Cardiovascular and Interventional Radiology Society of Europe (CIRSE), the Society of Interventional Radiology (SIR), the Korean Society of Interventional Radiology (KSIR), the Japanese Society of Interventional Radiology (JSIR), and the Chinese Society of Interventional Radiology (CSIR). The survey was distributed in English and Chinese. Statistical analysis was performed using Fisher's exact test and Chi-square test with Bonferroni correction. A p value of < 0.05 was considered statistically significant.

Data regarding the preferred procedure (DEB-TACE, cTACE, etc.) for single and multiple HCCs, cytotoxic agent and dosing, procedural end point, use of antibiotics, follow-up time and modality, and tumor response criteria were statistically different and have been published previously.

Results

An estimated total of 15,704 surveys were distributed and 1160 responses were obtained from 62 countries, leading to a response rate of 7.4%. Responses answering less than 90% of the survey were excluded ($n = 58$). Five hundred sixty-six respondents (51.4%) were members of SIR, 331 (30.0%) of CIRSE, 120 (10.9%) of CSIR, 58 (5.3%) of JSIR, and 27 (2.4%) KSIR (Fig. 1).

Respondents most commonly worked at an academic practice (397/1074, 37.0%), followed by a government hospital (300/1074, 27.9%), community hospital (175/1074, 16.3%), and a secondary/tertiary referral center (202/1074, 18.8%).

Ethiodized Oil Mixture

There was a statistically significant difference between the regions in amount of ethiodol oil used, among those that performed cTACE ($p < 0.0001$). Respondents most frequently use greater than 7.5 ml of ethiodol oil per procedure (240/506, 47.4%). Ninety-eight (19.3%) indicated the use of less than 5 ml of oil, 81 (16.0%) use 5–7.5 ml of oil, and 47 (9.3%) use greater than 10 ml of oil. Compared to the other societies, JSIR used significantly less oil in the emulsion ($p < 0.01$).

Of those who provided an approximate ratio of ethiodol oil to water-soluble cytotoxin, 145/396 (39.3%) used a higher oil to cytotoxin ratio, 168 (45.5%) used equal parts

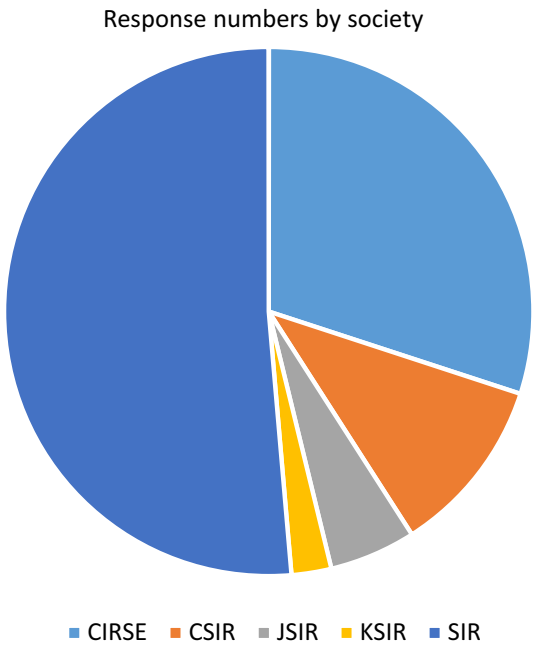

Fig. 1 *CIRSE* Cardiovascular and Interventional Radiology Society of Europe, *CSIR* Chinese Society of Interventional Radiology, *JSIR* Japanese Society of Interventional Radiology, *KSIR* Korean Society of Interventional Radiology, *SIR* Society of Interventional Radiology

oil and cytotoxin, and 56 (15.2%) used more cytotoxin than oil in their emulsion. The ratio of ethiodol oil to water-soluble cytotoxin varied significantly by society ($p < 0.001$) with those in KSIR being much more likely to use a higher oil to cytotoxin ratio than those in CIRSE and SIR.

Regarding the mixing process, the majority of respondents indicated that there was no method of preferential mixing (249/505, 49.3%). On the other hand, CSIR members statistically preferred to inject the cytotoxin into the ethiodol (57/120, 47.5%, $p < 0.01$).

Embolic Agent Type

The use of embolic agent for cTACE or TAE was statistically different among societies ($p < 0.0001$). Of the respondents that used embolic agents, spherical embolic particles were slightly favored (363/757, 47.9%), followed closely by gelatin-based or sponge particles (279/680, 36.8%). Non-spherical polyvinyl alcohol particles were used by 115 respondents (15.2%). KSIR and JSIR members almost exclusively used gelatin-based embolic particles (79/82, 96.3%), which was statistically different compared to other societies ($p = 0.0001$).

199 DEB-TACE users reported the use of secondary embolic agents at the end of their procedure if their procedural end point (near stasis, complete stasis, etc.) was not met following injection of the DEBs.

Drug-Eluting Bead Selection

Overall, LC/DC beads® (BTG, London, UK) were most popular among respondents (468/747, 62.7%), followed by Quadraspheres/Hepaspheres® (Merit Medical, South Jordan, Utah) (108, 14.4%), Tandem/Oncozene™ (Boston Scientific, Marlborough, Massachusetts) (99, 13.2%), and LifePearl (Terumo, Tokyo, Japan) (41, 5.5%). LC/DC® was statistically preferred by SIR members as compared to all other regions ($p = 0.01$).

Bead size preference was 100–300 μm in the majority of responses (354/690, 51.3%), followed by bead diameter less than 100 μm (243, 35.2%), 300–500 μm (42, 6.1%), and 500–800 μm (5, 0.7%). A combination of beads was reported 46 times (6.6%). There was no significant difference in the size of bead used between societies ($p = 0.07$).

Use of Additives

Additives including contrast, water, solubility agents, and lidocaine were preferentially used by SIR members (342, 61.1%) over CIRSE (145, 48.0%), CSIR (39, 34.8%), JSIR (16, 31.4%), and KSIR (11, 44.0%) ($p < 0.0001$).

Discussion

Since two randomized controlled trials demonstrated the superiority of TACE to supportive care, it has been a mainstay of treatment for unresectable HCCs [11, 12]. Despite coming to the same conclusion, these two groundbreaking works demonstrated significant procedural variability. While TA(C)E remains a common palliative treatment option for HCC, the degree of procedural variability is notable. While some degree of heterogeneity is expected in complex procedures, technical variation among geographic areas was found in even the most basic aspects of the procedure [10].

In cTACE, an emulsion is created when the cytotoxic drugs and ethiodized oil are mixed. It has been shown that the physical method of combining these agents leads to changes in droplet size, viscosity, cytotoxic drug release, and downstream distribution [13, 14]. Some data suggests that a water-in-oil emulsion achieves the best embolic effect and cytotoxin carriage capacity, and is currently recommended by expert technical recommendations [6, 15]. Despite the potential importance of oil and cytotoxic drug mixing, most respondents did not have a preferential method of mixing (249/505, 49.3%). Although not addressed by this survey, it is possible no preferential mixing method is used because the operator, despite the aforementioned data and the current recommendations, does not see this step as an influential factor on outcomes

[6]. The results of this survey also demonstrated that the most common amount of oil used per procedure was 7.5–10 ml, except in Japan, where interventionalists favored smaller amounts (0–5 ml). Most responses favored a 1:1 ratio of cytotoxin to oil. These results were unexpected, as preclinical work would suggest they result in sub-optimal embolization and drug release [15]. A possible explanation is lack of operator knowledge regarding the ideal chemical composition for favorable embolization, or a belief that the data is inconclusive.

There are multiple embolic agents that have been described for both cTACE and TAE. This study demonstrated a significant difference in the preferred type of particle among geographical location with gelfoam being more commonly used by members of JSIR, KSIR, CSIR and spherical particles by SIR members. The lack of consistency may be due to a lack of evidence showing superiority of one embolic over the other. Animal studies have shown that size of PVA particles did not affect the plasma doxorubicin levels [16]. Similarly, no embolic agent has been shown to be superior in head-to-head trials [17]. Some data suggests that smaller embolic agents may be able to have increased and more consistent tumor bed penetration, leading to complete necrosis of large HCC lesions. However, there are mixed results regarding complications of various bead sizes [18–20]. Embolic agents are not typically used in DEB-TACE procedures, as the beads act as an embolic agent. However, 199 respondents that favored the use of DEB-TACE mentioned that embolic agents are often added at the end of their procedure if their procedural end point (near stasis, complete stasis, etc.) was not met after injecting the DEBs.

Our study found that LC/DC beads were most commonly used. A recent in vitro study demonstrated the variable elution amounts, rates of release, diameter shrinkage, and times in suspension varied by product [21]. The choice of bead may be influenced by the respondents' preference, although cost and availability likely play an important role in this choice. To date, no in vivo study has reported increased efficacy in comparing bead types. Additionally, a study comparing efficacy of beads would have to be heavily scrutinized to ensure all other technical factors are similar.

In this study, 100–300 um beads were most commonly used. The preferred smaller size of beads may be related to the optimal selectivity and the release rate of cytotoxin [16, 22, 23]. However, there is a roll for larger beads; they can be helpful to avoid placement within significant arterioportal or hepatic venous shunts [24], but have also been shown to have an increased plasma concentration of cytotoxic drugs [25].

This study has several limitations. In order to promote busy practitioners to answer questions, the survey was written short and with multiple choice questions. Additional technical factors, such as type of intra-procedural imaging used, were excluded to limit survey questions. While this allowed for greater distribution compared with prior studies [7–9], answers regarding the most technical aspects of this study, as well as reasoning behind the respondents' choice, were not obtained. It should also be noted that surveys are prone to response bias. Additionally, the majority of responses were from only two societies (SIR and CIRSE).

In conclusion, there is a high variability of practitioner methodology in the use of TA(C)E in the treatment of HCC. Further randomized controlled trials are needed to guide practioners as to what technical methods provide the greatest therapeutic benefits.

Acknowledgements The authors would like to acknowledge Dr. Yasuaki Arai, Dr. Gaojun Teng, Dr. Young Soo Do, Dr. Hyun-Ki Yoon, Dr. Daniel Brown, and Dr. Charles Ray for their feedback and comments in the preparation of the survey. Guarantor: The scientific guarantor of this publication is Paul Craig. Statistics and biometry: Scott Lunos kindly provided statistical advice for this manuscript.

Compliance with Ethical Standards

Conflict of interest The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

Informed Consent Informed consent was not required because this was a survey of practicing interventional radiologists.

Ethical Approval Institutional Review Board approval was not required because this was a survey of practicing interventional radiologists.

Appendix: Survey Text

Transcatheter Arterial (Chemo)embolization (TA(C)E) Survey

This *short* (one-page) survey should not take more than 2 min of your time. This survey was designed to obtain a general idea of the type of TA(C)E procedures that you typically perform. It is important to answer at least one answer per question, as follow-up questions may drop down. Thank you very much for your participation.

1. What country do you practice in?
    a. (Answer field blank)
2. What type of practice are you in?
    a. Academic
    b. Private practice – community hospital
    c. Private practice – secondary or tertiary referral center
    d. Government hospital
    e. Other (please specify)
        i. (Answer field blank)

3. For TA(C)E procedures at your institution, what is the common cytotoxic agent used for the treatment of hepatocellular carcinoma (HCC)?
   a. Doxorubicin
   b. Epirubicin
   c. Cisplatin
   d. Mitoxantrone
   e. Mitomycin C
   f. SMANCS
   g. Pirarubicin
   h. Nemorubicin
   i. Miriplatin
   j. Idarubicin
   k. Irinotecan
   l. Anthracycline (e.g., Doxorubicin, Epirubicin) and Mitomycin C
   m. Anthracycline and Cisplatin
   n. Anthracycline, Mitomycin C, and Cisplatin
   o. None of the above (bland transarterial embolization (TAE))
   p. Other (please specify)
4. For TA(C)E procedures at your institution, how is the dose of cytotoxin agent determined?
   a. Fixed dose (e.g., 50 mg Doxorubicin for every person). Please list dose below.
   b. Body weight (e.g., 1 mg Doxorubicin for every kg). Please list amount per kg below.
   c. Body surface area (e.g., 50 mg/meter^2). Please list amount per meter^2 below.
   d. Tumor size
   e. Liver function (AFP, etc.)
   f. Other (please specify)
5. What is your typical procedure for a single HCC?
   a. Ethiodized oil TACE (cTACE)
   b. Drug-Eluting Beads TACE
   c. Bland Transarterial Embolization (TAE)
   d. Technique depends on the extension and location of the tumor
   e. Other (please specify)
6. (What amount of ethiodized oil is typically used?
   a. Not applicable
   b. 0–5 ml
   c. 5–7.5 ml
   d. 7.5–10 ml
   e. > 10 ml
   f. Other
7. What is the ratio (volume:volume) of ethiodized oil to cytotoxic agent used in your procedure?
8. How is the ethiodized oil mixed with the cytotoxic agent?
   a. Not applicable
   b. Pump between stop cock (to and fro)—ethiodized oil tube injected into cytotoxin tube
   c. Pump between stop cock (to and fro)—cytotoxin tube injected into ethiodized oil
   d. Pump between stop cock (to and fro)—no preference in order mixed
   e. Mixed with a machine
   f. No specific method
   g. Other (please specify)
9. What type of drug-eluting beads do you use?
   a. Not applicable
   b. Tandem
   c. Pearl
   d. QuadraSpheres
   e. LC/DC
   f. Other (please specify)
10. What size of drug-eluting beads do you use (please specify)?
    a. (Answer field blank)
11. What is your procedural end point?
    a. Administration of fixed dose
    b. Flow reduction in the feeding vessel(s)
    c. Complete stasis in the feeding vessel(s)
    d. Oil uptake by tumor
    e. A combination of B and D or C and D
    f. Other (please specify)
12. Are embolic agents used in your procedure?
    a. No
    b. Yes—Gelatin (specify product below)
    c. Yes—Non-spherical polyvinyl alcohol (specify product below)
    d. Yes—Spherical (specify product below)
13. What is your typical procedure for multiple HCCs?
    a. Ethiodized oil TACE (cTACE)
    b. Drug-Eluting Beads TACE
    c. Bland Transarterial Embolization (TAE)
    d. Technique depends on the extension and location of the tumor
    e. Other (please specify)
14. Are additives used with the primary cytotoxic agent (water-soluble contrast, solubility agents, etc.)?
    a. No
    b. Yes (please specify)

15. Do you routinely use antibiotics with TA(C)E procedures?
    a. No
    b. Yes, before
    c. Yes, during
    d. Yes, after
    e. A combination of the factors listed above
16. When is your typical clinical follow-up for TA(C)E procedures?
    a. Less than 2 weeks
    b. 2 weeks–1 month
    c. > 1 month–< 2 months
    d. > 2 months
17. What type of imaging follow-up do you perform?
    a. CT (specify interval below)
    b. MR (specify interval below)
    c. Other (please specify below)
18. What criteria do you use to determine tumor response?
    a. European Association of the Study of Liver (EASL)
    b. World Health Organization (WHO)
    c. Response Evaluation Criteria in Solid Tumors (RECIST)
    d. Modified Response Evaluation Criteria in Solid Tumors (mRECIST)
    e. Other (please specify).

References

1. Torre LA, Siegel RL, Ward EM, Jemal A. Global cancer incidence and mortality rates and trends—an update. Cancer Epidemiol Prev Biomark. 2016;25(1):16–27.
2. Lai CL, Lok ASF, Wu PC, Chan GCB, Lin HJ. Doxorubicin versus no antitumor therapy in inoperable hepatocellular carcinoma. A prospective randomized trial. Cancer. 1988;62(3):479–83.
3. Varela M, Real MI, Burrel M, et al. Chemoembolization of hepatocellular carcinoma with drug eluting beads: efficacy and doxorubicin pharmacokinetics. J Hepatol. 2007;46(3):474–81.
4. Hong K, Khwaja A, Liapi E, Torbenson MS, Georgiades CS, Geschwind J-FH. New intra-arterial drug delivery system for the treatment of liver cancer: preclinical assessment in a rabbit model of liver cancer. Clin Cancer Res. 2006;12(8):2563–7.
5. Kan Z, Sato M, Ivancev K, et al. Distribution and effect of iodized poppyseed oil in the liver after hepatic artery embolization: experimental study in several animal species. Radiology. 1993;186(3):861–6.
6. de Baere T, Arai Y, Lencioni R, et al. Treatment of liver tumors with lipiodol TACE: technical recommendations from experts opinion. Cardiovasc Intervent Radiol. 2016;39(3):334–43.
7. Gaba RC. Chemoembolization practice patterns and technical methods among interventional radiologists: results of an online survey. Am J Roentgenol. 2012;198(3):692–9.
8. Bargellini I, Florio F, Golfieri R, Grosso M, Lauretti DL, Cioni R. Trends in utilization of transarterial treatments for hepatocellular carcinoma: results of a survey by the Italian Society of Interventional Radiology. Cardiovasc Intervent Radiol. 2014;37(2):438–44.
9. Gaba RC, Baerlocher MO, Nikolic B, Venkatesan AM, Lewandowski RJ. Clinical and imaging follow-up practices after transarterial therapy for primary and secondary hepatic malignancies: results of an online survey. Acad Radiol. 2015;22(12):1510–5.
10. Young S, Craig P, Golzarian J. Current trends in the treatment of hepatocellular carcinoma with transarterial embolization: a cross-sectional survey of techniques. J Eur Radiol. 2018;1:2. https://doi.org/10.1007/s00330-018-5782-7.
11. Llovet JM, Real MI, Montaña X, et al. Arterial embolisation or chemoembolisation versus symptomatic treatment in patients with unresectable hepatocellular carcinoma: a randomised controlled trial. Lancet. 2002;359(9319):1734–9.
12. Lo CM, Ngan H, Tso WK, et al. Randomized controlled trial of transarterial lipiodol chemoembolization for unresectable hepatocellular carcinoma. Hepatology. 2002;35(5):1164–71.
13. Raoul J, Heresbach D, Bretagne J, et al. Chemoembolization of hepatocellular carcinomas a study of the biodistribution and pharmacokinetics of doxorubicin. Cancer. 1992;70(3):585–90.
14. Nakamura H, Hashimoto T, Oi H, Sawada S. Transcatheter oily chemoembolization of hepatocellular carcinoma. Radiology. 1989;170(3):783–6.
15. Kan Z, Wright K, Wallace S. Ethiodized oil emulsions in hepatic microcirculation: in vivo microscopy in animal models. Acad Radiol. 1997;4(4):275–82.
16. Lee K-H, Liapi E, Ventura VP, et al. Evaluation of different calibrated spherical polyvinyl alcohol microspheres in transcatheter arterial chemoembolization: VX2 tumor model in rabbit liver. J Vasc Interv Radiol. 2008;19(7):1065–9.
17. Koçyiğit A, Dicle O, Göktay Y, Astarcıoğlu İ. The effect of using different embolic agents on survival in transarterial chemoembolization of hepatocellular carcinoma: gelfoam versus polyvinyl alcohol. Diagn Interv Radiol. 2014;20(4):323.
18. Bonomo G, Pedicini V, Monfardini L, et al. Bland embolization in patients with unresectable hepatocellular carcinoma using precise, tightly size-calibrated, anti-inflammatory microparticles: first clinical experience and one-year follow-up. Cardiovasc Intervent Radiol. 2010;33(3):552–9.
19. Stampfl S, Bellemann N, Stampfl U, et al. Inflammation and recanalization of four different spherical embolization agents in the porcine kidney model. J Vasc Interv Radiol. 2008;19(4):577–86.
20. Malagari K, Pomoni M, Spyridopoulos TN, et al. Safety profile of sequential transcatheter chemoembolization with DC Bead™: results of 237 hepatocellular carcinoma (HCC) patients. Cardiovasc Intervent Radiol. 2011;34(4):774–85.
21. de Baere T, Plotkin S, Yu R, Sutter A, Wu Y, Cruise GM. An in vitro evaluation of four types of drug-eluting microspheres loaded with doxorubicin. J Vasc Interv Radiol. 2016;27(9):1425–31.
22. Martin R, Irurzun J, Munchart J, et al. Optimal technique and response of doxorubicin beads in hepatocellular cancer: bead size and dose. Korean J Hepatol. 2011;17(1):51.
23. Lee K-H, Liapi E, Vossen JA, et al. Distribution of iron oxide—containing Embosphere particles after transcatheter arterial embolization in an animal model of liver cancer: evaluation with MR imaging and implication for therapy. J Vasc Interv Radiol. 2008;19(10):1490–6.

24. Lencioni R, De Baere T, Burrel M, et al. Transcatheter treatment of hepatocellular carcinoma with Doxorubicin-loaded DC Bead (DEBDOX): technical recommendations. Cardiovasc Intervent Radiol. 2012;35(5):980–5.
25. Lewis AL, Taylor RR, Hall B, Gonzalez MV, Willis SL, Stratford PW. Pharmacokinetic and safety study of doxorubicin-eluting beads in a porcine model of hepatic arterial embolization. J Vasc Interv Radiol. 2006;17(8):1335–43.