Development of Intra-Arterial Chemoembolization for Various Types of Cancer in Humans

RYOHEI KUWATSURU*¹⁾, SHINICHI HORI*²⁾

*¹⁾ Department of Radiology, Juntendo University Faculty of Medicine, Tokyo, Japan, *²⁾ Department of Radiology, Gate Tower Institute for Image Guided Therapy, Osaka, Japan

Intra-arterial chemoembolization has been performed for more than 30 years as a standard anti-cancer therapy for unresectable cases of hepatocellular carcinoma. Recent developments in diagnostic machines and the advent of micro-catheters, micro-guidewires, and new embolic agents (such as microspheres) have enabled this technique to be used for the treatment of other tumors, such as lung cancer, breast cancer, liver metastasis, lung metastasis, lymph node metastasis, and bone metastasis. This review article describes these developments in intra-arterial chemotherapy, with a focus on liver tumors and pulmonary tumors.

Key words: transarterial chemoembolization, hepatocellular carcinoma, liver metastasis, pulmonary tumor, computed tomography during angiography

Introduction

Intra-arterial chemotherapy, i.e., direct infusion of anticancer drugs to a tumor-feeding artery, has been performed for many cancers¹⁾⁻⁴⁾. High-density injection of anticancer drugs into tumors through arteries has the potential to induce a strong chemotherapeutic effect; however, intra-arterial chemotherapy is not popular for most cancers because of the difficulty of the procedure.

Recent developments in micro-catheters and micro-guidewires have enabled superselective catheter insertion and injection of anti-cancer drugs directly into the tumor-feeding artery (i.e., avoiding adjacent normal tissue)¹⁾⁻³⁾. Small embolic agents such as microspheres are now available to embolize the tumor-feeding arteries during or after injection of anti-cancer drugs to enhance the drug effect^{5) 6)}. Even simply blocking tumor-feeding arteries with small embolic agents, without anti-cancer drugs, sometimes has anti-cancer effects due to ischemia, especially in vascular-rich tumors⁷⁾⁻¹⁰⁾.

Angiography accompanied with computed tomography (CT) is suitable to confirm the precise distribution of anti-cancer drugs. Recently, reconstruction of CT-like images from 4-dimensional fluoroscopic data using cone-beam CT, has become available in some angiographic machines to confirm the distribution area and to facilitate precise arterial embolization¹¹⁾⁻¹³⁾. In this review article, developments in intra-arterial chemotherapy are described.

Micro-catheters and micro-guidewires

Catheters used about 30 years ago were mostly 6-7 Fr (diameter, 2-2.3 mm) or sometimes larger. These large catheters were difficult to insert into small arteries, and troubles at the puncture site, such as bleeding, hematoma, and pseudoaneurysm, were frequent. Because precise insertion of the catheter into small arteries was impossible, precise transarterial chemoembolization was not performed. The development of catheter introducers to help control catheter movement has lessened the

Corresponding author: Ryohei Kuwatsuru

Department of Radiology, Juntendo University Faculty of Medicine
2-1-1 Hongo, Bunkyo-ku, Tokyo 113-8421, Japan

TEL: +81-3-3813-3111 FAX: +81-3-3812-3738 E-mail: kuwatsuru@juntendo.ac.jp

35th Health Topics for Tokyoites: The Cutting Edge of Intravascular Treatment [Held on Feb. 21, 2015]

[Received July 8, 2015]

Figure-1 Micro-catheter and micro-guidewire

An example micro-catheter (arrow; 0.7 mm in diameter) and micro-guidewire (arrowhead; 0.4 mm in diameter); both are thin enough to enter the small tumor-feeding arteries such as small hepatic arteries.

trouble at puncture sites. Catheter size has also been reduced, with 4-5 Fr (diameter, 1.3-1.7 mm) catheters becoming mainstream.

Furthermore, micro-catheters (1.6-2.7 Fr; diameter, 0.5-0.9 mm) and micro-guidewires (0.010-0.016 inches; diameter, 0.3-0.4 mm) have been invented (Figure-1); each of these inserts into the catheter and enters the small arteries through the tip of the catheter. Several sizes of micro-catheters are now widely used, and superselective embolization has become relatively easy.

Microspheres

For more than 40 years, transcatheter chemoembolization has been performed for hepatocellular carcinoma (HCC) with the use of oily contrast medium (lipiodol) or lipiodol plus anticancer drug emulsion and sponge-based embolic materials that dissolve within two weeks after injection¹⁴⁾⁻¹⁷⁾. Lipiodol passes easily through the small arteries to the targeted lesion. Lipiodol accumulation depends on the arterial flow: it accumulates particularly well in vascular-rich HCCs, but its accumulation in the normal liver tissue has little detrimental effect because it washes out in two weeks. Sponge-based embolic materials are additionally used to extend the time of embolization. Because the sponge-based material is large and its size is inconsistent, precise embolization of the tumor and tumor-feeding arteries is difficult. Furthermore, since the diameter of the sponge is larger than that of the tumor-feed-

Figure-2 Microscopic features of Embospheres (diameter, 100-300 μ m)

Embospheres, one of the microsphere particles are smooth-surfaced, spherical, and relatively uniform in size.

(Courtesy of Nihon Kayaku KK)

ing arteries, embolization usually occurs due to the blockade of the proximal tumor-feeding arteries. In some such cases, collateral arteries develop and arterial blood flow communicates to the distal site of the tumor-feeding artery; this results in wash out of lipiodol or lipiodol plus anti-cancer drug emulsion—the tumor fed by the new collateral arteries remains alive.

Because microspheres are small with little variation in size (Figure-2), tumors and tumor-feeding arteries are embolized precisely without proximal embolization. Also, because some anti-cancer drugs can be embedded in the microspheres, drugs can be released gradually, making their effects stronger and more sustained. Microsphere embolization just after infusion of anticancer drugs is also common choice for chemoembolotherapy.

CT during angiography

After injection of the contrast agent in angiography, it is sometimes difficult to evaluate whether a tumor is enhanced or not if there is only faint enhancement. Strongly enhanced tumors are easy to recognize, but differentiation of the tumor from normal hypervascular tissue is sometimes difficult. Transcatheter arterial chemoembolization (TACE) with microspheres is successful if the anticancer drug and embolic agent distributes only to the lesion; however, if a large volume of normal tissue is included in the embolic area, severe infarction or inflammation may occur in normal tissue and

Figure-3 Angiography with computed tomography (CT)
Angiography with CT allows CT to be performed during angiography at the same time.

sometimes this becomes serious.

IVR-CT (Figure-3) can take CT images during arterial infusion of contrast agents (CT during angiography) which precisely show the distribution of each artery, and it helps with planning which arteries should or should not be embolized. Sometimes there are multiple tumor-feeding arteries with each artery feeding a different part of the tumor, so that embolization of several arteries is required. Newly developed angiography machines called cone-beam CT can reconstruct the data to show CT-like images; this is also useful for determining the distribution of the tumor-feeding arteries¹¹⁾⁻¹³⁾.

Treatment of tumors with TACE

Theoretically, TACE can be performed for any cancer; however, because of potential adverse effects, application of this treatment should be performed carefully. Microspheres are permanent materials and cause embolization of non-target organs such as gallbladder, pancreas, stomach, duodenum, and other digestive organs if injected into inappropriate arteries. Liver cancer, including HCC and liver metastases, is one of the best lesions to be treated by TACE because the hepatic double blood supply (80% portal vein feeding and 20% hepatic arterial feeding) means that non-target embolization of hepatic arteries in normal liver parenchyma does not induce serious problems. The situation with lung cancer is nearly the same as that with liver cancer because lung is perfused by both bronchial arteries and pulmonary arteries. Other

solid tissues such as breast, kidney, lymph node, and bone are also candidates for transarterial chemoembolization. Even cancers of the stomach, colon, and other digestive organs are candidates for this therapy; however, careful selective injection to the target lesions without non-target embolization is required to avoid severe adverse events such as perforation of the digestive organs and pancreatitis.

Two protocols for TACE with microspheres, monthly and on demand, are commonly used. Once TACE with microspheres is planned and performed, the patient is discharged within 3 days after the procedure and evaluated one month after the procedure, followed by a second TACE with microspheres. The therapy can be repeated on demand after evaluation with CT. If the therapy is not effective, the type of anti-cancer drugs will be changed. Because the side effects to other parts of the body, such as the bone marrow, skin, and gastrointestinal tract, are minimal, patients receiving this therapy have a better quality of life than those receiving systemic chemotherapy.

HCC and liver metastasis

The usefulness of hepatic arterial chemoembolization for HCC was first reported by Yamada *et al.* in 1983¹⁴⁾. They performed TACE for unresectable HCCs and observed that the 1-year survival rate (44%) was much better than that of surgery (28%) at that time. They used 1-2 mm pieces of gelatin sponges embedded with 10 mg of mitomycin C or 20 mg of Adriamycin (doxorubicin hydrochloride) for the therapy. They also performed embolization therapy for various malignant tumors other than HCC, such as lung cancer, renal cell carcinoma, uterine cancer, and bladder cancer, and observed that the best result was obtained with HCC. Also in 1983, Nakamura¹⁵⁾ reported a case of resected HCC after TACE (Adriamycin infusion immediately followed by gelatin infusion) and described that good results were obtained for small, thickly-encapsulated lesions located at sites remote from collateral circulation. In both reports, complications such as gangrenous cholecystitis were severe due to the wide distribution of embolization, including of the cystic artery. Oily chemoembolization, reported by Nakamura in 1989, which used a mixture of dissolved doxorubicin and iodized oil (lipiodol)

Figure-4 HCC before and after superselective TACE

A. HCC (arrow) is well enhanced after bolus injection of contrast media.

B. After the superselective TACE, lipiodol accumulation is clearly visualized as white area in the tumor.

followed by gelatin sponge particles, is the model for the currently performed “conventional TACE (cTACE)”¹⁶⁾. “Segmental TACE”¹⁷⁾, “subsegmental TACE”¹⁸⁾, and “ultraselective TACE”¹⁹⁾ arterial embolization, which have better therapeutic effects and fewer complications than cTACE, have arisen with the development of improved catheter technique and the advent of micro-catheters. Patients undergoing selective TACE have been shown to have better survival rates than those subjected to non-selective embolization²⁰⁾. A prospective, single-arm, controlled study of TACE for unresectable HCC showed a good response rate of 73% (complete response [CR], 42%; partial response [PR], 31%) and an excellent 2-year survival rate of 75%²¹⁾. Lipiodol is used as the liquid contrast agent not only to embolize the tumor but also to embolize the area surrounding the tumor and the portal vein near the tumor where extratumoral invasion frequently occurs (Figure-4). The therapeutic effect is strong because the tumor and its surrounding area, which contains extracapsular invasions and daughter nodules, are embolized simultaneously. Sponge particles are useful to retain the lipiodol longer and to strengthen the anti-tumor effect. The role of the choice of chemotherapeutic drug in TACE is uncertain^{22) 23)}, and is to be confirmed in the future.

Microspheres are now used as the embolic agent in both bland embolization (which uses embolic agent only) and TACE with drug-eluting microspheres (which uses embolic agent impregnated with chemotherapeutic drugs such as doxorubicin and epirubicin). In bland embolization, the main treatment mechanism is the ischemic effect, which

induces a reduction in tumor size. Because HCC is fed only by the hepatic artery, bland embolization with microspheres is effective for unresectable HCC due to the embolization of the tumor and small tumor-feeding artery, and it causes less severe liver and biliary damage than TACE⁷⁾⁻¹⁰⁾ thereby minimizing post-embolization syndrome. Bland embolization tends to preserve the arterial patency even after several repeat sessions²⁴⁾. There have been no reports comparing the efficacy of bland embolization with that of cTACE. The efficacy of TACE using drug-eluting beads (DEB-TACE) seems superior to that of bland embolization with microspheres^{25) 26)}; however, liver damage is less with bland embolization²⁶⁾.

Comparison of the efficacy between cTACE and DEB-TACE for HCC is controversial, and no statistically significant differences have been reported to date²⁷⁾⁻²⁹⁾. cTACE and microsphere embolization can be beneficial for different applications. Microspheres can embolize the tumor and tumor feeding arteries more tightly than can gelatin sponge; however, because lipiodol is a liquid agent, it reaches not only the tumor, but also the peritumoral area and the nearby portal vein. Since HCCs sometimes have satellite lesions and extracapsular invasion, accumulation and blockade of the surrounding area of HCC by embolic agents such as lipiodol has a superior tumor necrosis effect to other embolic agents such as microspheres and gelatin sponge particles. Bland embolization with microspheres is an effective therapy for large hypervascular HCCs, because stopping arterial flow will cause necrosis of most of the tumor in these cases. Small residual tumors which remained after first

Figure-5 Gastric cancer with liver metastases

The huge liver metastasis (arrow) had rim enhancement on contrast-enhanced CT before TACE with docetaxel-loaded microspheres (A) and became small with little enhancement 2 months after the initial TACE (B). Hepatic angiography showed perfusion of the tumor in the right lobe of the liver before TACE (C) whereas there was almost no perfusion after TACE (D).

treatment by bland embolization, are treated in a second session when the tumor is too large to treat one session.

One good candidate for DEB-TACE might be liver metastasis (Figure-5). Seki *et al.* reported the case receiving the TACE with docetaxel-loaded microspheres who had liver metastases from colorectal cancer that were refractory to the current systemic chemotherapy³⁰⁾. After 3 courses of TACE, tumor marker had decreased and PR was obtained by RECIST criteria. Huppert *et al.* performed a prospective study of TACE with irinotecan-eluting microspheres for colorectal cancer liver metastases in a salvage setting and showed this treatment to be safe but provided only limited efficacy: the median time to progression was 5 months and median overall survival after first TACE was 8 months³¹⁾. Changing the drug and decreasing the size of microspheres is being considered to improve the effectiveness of this type of treatment.

Lung cancer and pulmonary metastasis

Currently, the use of TACE for lung tumor therapy has not been widely accepted due to the lack of enough clinical experience. Bronchial artery embolization is performed commonly for patients with hemoptysis; it effectively improves symptoms including bleeding from primary lung cancer and pulmonary metastases and benign lesions^{32) 33)}. Park *et al.* reported the result of arterial embolization for primary lung cancer patients with hemoptysis³²⁾. Though the technical success rate was 100%, and the clinical success rate was 79%, the rate of recurrence of hemoptysis was high (33%). For malignant lesions, both stopping the bleeding and shrinkage of the tumor by chemotherapy are necessary to stop the hemoptysis without recurrence.

Bronchial arterial infusion (BAI) therapy is the infusion of chemotherapeutic agents into the bronchial artery and other associated systemic arteries. This therapy was introduced about 50 years ago for advanced lung cancer patients who

Figure-6 Pulmonary cancer with mediastinal lymph node metastases

Right bronchial arteriography showed tumor perfusion in a mediastinal lymph node behind the superior vena cava (A), which was confirmed by CT during angiography (B). Right internal thoracic arteriography showed tumor perfusion at the mediastinal lymph node ventral to the superior vena cava (C) which was confirmed by CT during angiography (D). CT before TACE showed narrowing of the superior vena cava (arrow; E) and narrowing improved due to the volume reduction of the mediastinal lymph nodes 3 months after TACE (F).

could not be treated with surgery, chemotherapy, or radiation therapy, and it was reappraised as a preoperative adjuvant therapy for advanced hilar stage IIIA and IIIB lung cancer in 1990¹⁾. In one report, BAI with cis-diamminedichloroplatinum had a PR rate of 67% for locally advanced non-small cell lung cancer²⁾ and had a CR of 100% for centrally located early-stage lung cancer³⁾. The advantage of BAI therapy for lung cancer is that a high concentration of chemotherapeutics reaches the lesion even though the infusion dose is less than systemic therapy; this means that the therapy can be repeated many times, and the systemic and local side effects are minimal.

The anatomy of bronchial arteries varies between people³⁴⁾ and lung cancer is fed not only by bronchial arteries but also by systemic arteries such as the internal thoracic artery, intercostal artery, and lateral thoracic artery. Therefore, detection of tumor-feeding arteries is important. Nakanishi reported the usefulness of multi-arterial infusion chemotherapy for patients with advanced non-small cell lung cancer³⁵⁾. In their study, 1 (3%) CR and 16 (50%) PR were obtained with gemcitabine plus cisplatin as the first-line drug combina-

tion, with the exception that doxorubicin was used instead of cisplatin in patients with renal dysfunction and anorexia. They found 1 to 10 (mean $\pm$ SD, 3.8 ± 2.0) feeding arteries for lung tumors, 0 to 1 (mean $\pm$ SD, 0.7 ± 0.1) for hilar lymph node metastasis, and 0 to 2 (mean $\pm$ SD, 0.8 ± 0.1) for mediastinal lymph node metastasis. Stronger staining lung tumors and lymph node metastases by angiography showed a marked response. As mentioned above, we now can use CT during angiography, allowing more precise evaluation of tumor staining, and more distal catheter insertion is possible to avoid normal tissue damage.

The use of TAE with microspheres for pulmonary metastases from renal cell carcinoma has been reported³⁶⁾. The report showed the safety, local efficacy, and palliative effects of bronchial artery embolization with microspheres (superabsorbent polymer microspheres, SAP-MS), a micro-catheter, and CTA. The total response rates (PR+CR) at 1, 3, and 6 months after therapy were 38.8% (19/49), 44.9% (22/49), and 38.8% (19/49), respectively. Highly-enhanced lesions showed a high total response rate (90.9%) and 1-5 (median, 2.9) tumor-feeding arteries were successfully

embolized. After each cannulation of the tumor-feeding artery, CTA was performed and the distribution of contrast medium was confirmed. CTA, which is more accurate than angiography, was required to check abnormal enhancement of the spinal cord, left atria, and esophagus to avoid spinal cord injury, non-target embolization, and esophageal embolization. In our cases, some cases showed good response rate with DEB-TACE (Figure-6).

Conclusion

The advent of micro-catheters and micro-guide-wires, CT angiography apparatus, and new embolic materials such as microspheres has helped to make TACE more effective and widely applicable for human cancers.

References

- 1) Watanabe Y, Shimizu J, Murakami S, *et al*: Reappraisal of bronchial arterial infusion therapy for advanced lung cancer. *Jpn J Surg*, 1990; 20: 27-35.
- 2) Osaki T, Oyama T, Takenoyama M, *et al*: Feasibility of induction chemotherapy using bronchial arterial infusion for locally advanced non-small cell lung cancer: a pilot study. *Surg Today*, 2002; 32: 772-778.
- 3) Osaki T, Hanagiri T, Nakanishi R, Yoshino I, Taga S, Yasumoto K: Bronchial arterial infusion is an effective therapeutic modality for centrally located early-stage lung cancer; results of a pilot study. *Chest*, 1999; 115: 1424-1428.
- 4) Volovat SR, Volovat C, Negru SM, Danciu M, Scripcariu V: The efficacy and safety of hepatic arterial infusion of oxaliplatin plus intravenous irinotecan, leucovorin and fluorouracil in colorectal cancer with inoperable hepatic metastasis. *J Chemother*, 2015; May 27: 1973947815Y0000000042. [Epub ahead of print]
- 5) Lewis AL, Taylor RR, Hall B, Gonzalez MV, Wills 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: 1335-1343.
- 6) Lewis AL, Gonzalez MV, Lloyd AW, *et al*: DC bead: in vitro characterization of a drug-delivery device for transarterial chemoembolization. *J Vasc Interv Radiol*, 2006; 17: 335-342.
- 7) Covey AM, Maluccio MA, Schubert J, *et al*: Particle embolization of recurrent hepatocellular carcinoma after hepatectomy. *Cancer*, 2006; 106: 2181-2189.
- 8) Osuga K, Hori S, Hiraishi K, *et al*: Bland embolization of hepatocellular carcinoma using superabsorbent polymer microspheres. *Cardiovasc Intervent Radiol*, 2008; 31: 1108-1116.
- 9) Maluccio MA, Covey AM, Porat LB, *et al*: Transcatheter arterial embolization with only particles for the treatment of unresectable hepatocellular carcinoma. *J Vasc Interv Radiol*, 2008; 19: 862-869.
- 10) 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: 552-559.
- 11) Miyayama S, Yamashiro M, Okuda M, *et al*: Usefulness of cone-beam computed tomography during ultraselective transcatheter arterial chemoembolization for small hepatocellular carcinomas that cannot be demonstrated on angiography. *Cardiovasc Intervent Radiol*, 2009; 32: 255-264.
- 12) Miyayama S, Yamashiro M, Hashimoto M, *et al*: Identification of small hepatocellular carcinoma and tumor-feeding branches with cone-beam CT guidance technology during transcatheter arterial chemoembolization. *J Vasc Interv Radiol*, 2013; 24: 501-508.
- 13) Miyayama S, Yamashiro M, Hashimoto M, *et al*: Comparison of local control in transcatheter arterial chemoembolization of hepatocellular carcinoma ≤ 6 cm with or without intraprocedural monitoring of the embolized area using cone-beam computed tomography. *Cardiovasc Intervent Radiol*, 2014; 37: 388-395.
- 14) Yamada R, Sato M, Kawabata M, Nakatsuka H, Nakamura K, Takashima S: Hepatic artery embolization in 120 patients with unresectable hepatoma. *Radiology*, 1983; 148: 397-401.
- 15) Nakamura H, Tanaka T, Hori S, *et al*: Transcatheter embolization of hepatocellular carcinoma: assessment of efficacy in cases of resection following embolization. *Radiology*, 1983; 147: 401-405.
- 16) Nakamura H, Hashimoto T, Oi H, Sawada S: Transcatheter oily chemoembolization of hepatocellular carcinoma. *Radiology*, 1989; 170: 783-786.
- 17) Uchida H, Ohishi H, Matsuo N, *et al*: Transcatheter hepatic segmental arterial embolization using Lipiodol mixed with an anticancer drug and gelfoam particles for hepatocellular carcinoma. *Cardiovasc Intervent Radiol*, 1990; 13: 140-145.
- 18) Matsui O, Kadoya M, Yoshikawa J, *et al*: Small hepatocellular carcinoma: treatment with subsegmental transcatheter arterial embolization. *Radiology*, 1993; 188: 79-83.
- 19) Miyayama S, Matsui O, Yamashiro M, *et al*: Ultraselective transcatheter arterial chemoembolization with a 2-F tip microcatheter for small hepatocellular carcinomas: relationship between local tumor recurrence and visualization of the portal vein with iodized oil. *J Vasc Interv Radiol*, 2007; 18: 365-376.
- 20) Yamakado K, Miyayama S, Hirota S, *et al*: Hepatic arterial embolization for unresectable hepatocellular carcinomas: do technical factors affect prognosis? *Jpn J Radiol*, 2012; 30: 560-566.
- 21) Ikeda M, Arai Y, Park SJ, *et al*: Prospective study of transcatheter arterial chemoembolization for unresectable hepatocellular carcinoma: an Asian cooperative study between Japan and Korea. *J Vasc Interv Radiol*, 2013; 24: 490-500.
- 22) Camma C, Schepis F, Orlando A, *et al*: Transarterial chemoembolization for unresectable hepatocellular carcinoma: meta-analysis of randomized controlled trials. *Radiology*, 2002; 224: 47-54.
- 23) Llovet JM, Bruix J: Systematic review of randomized trials for unresectable hepatocellular carcinoma: chemo-

- embolization improves survival. *Hepatology*, 2003; 37: 429-442.
- 24) Erinjeri JP, Salhab HM, Covey AM, Getrajdman GI, Brown KT: Arterial patency after repeated hepatic artery bland particle embolization. *J Vasc Interv Radiol*, 2010; 21: 522-526.
- 25) Malagari K, Pomoni M, Kelekis A, *et al*: Prospective randomized comparison of chemoembolization with doxorubicin-eluting beads and bland embolization with BeadBlock for hepatocellular carcinoma. *Cardiovasc Intervent Radiol*, 2010; 33: 541-551.
- 26) Nicolini A, Martinetti L, Crespi S, Maggioni M, Sangiovanni A: Transarterial chemoembolization with epirubicin-eluting beads versus transarterial embolization before liver transplantation for hepatocellular carcinoma. *J Vasc Interv Radiol*, 2010; 21: 327-332.
- 27) Lammer J, Malagari K, Vogl T, *et al*: Prospective randomized study of doxorubicin-eluting-bead embolization in the treatment of hepatocellular carcinoma: results of the PRECISION V study. *Cardiovasc Intervent Radiol*, 2010; 33: 41-52.
- 28) Sacco R, Bargellini I, Bertini M, *et al*: Conventional versus doxorubicin-eluting bead transarterial chemoembolization for hepatocellular carcinoma. *J Vasc Interv Radiol*, 2011; 22: 1545-1552.
- 29) Golfieri R, Giampalma E, Renzulli M, *et al*: Randomised controlled trial of doxorubicin-eluting beads vs conventional chemoembolisation for hepatocellular carcinoma. *Br J Cancer*, 2014; 111: 255-264.
- 30) Seki A, Hori S: Transcatheter arterial chemoembolization with docetaxel-loaded microspheres controls heavily pretreated unresectable liver metastases from colorectal cancer: a case study. *Int J Clin Oncol*, 2011; 16: 613-616.
- 31) Huppert P, Wenzel T, Wietholtz H: Transcatheter arterial chemoembolization (TACE) of colorectal cancer liver metastases by Irinotecan-eluting microspheres in a salvage patient population. *Cardiovasc Intervent Radiol*, 2014; 37: 154-164.
- 32) Park HS, Kim YI, Kim HY, Zo JI, Lee JH, Lee JS: Bronchial artery and systemic artery embolization in the management of primary lung cancer patients with hemoptysis. *Cardiovasc Intervent Radiol*, 2007; 30: 638-643.
- 33) Chen J, Chen LA, Liang ZX, *et al*: Immediate and long-term results of bronchial artery embolization for hemoptysis due to benign versus malignant pulmonary diseases. *Am J Med Sci*, 2014; 348: 204-209.
- 34) Walker CM, Rosado-de-Christenson ML, Martinez-Fimenez S, Kunin JR, Wible BC: Bronchial arteries: anatomy, function, hypertrophy, and anomalies. *Radiographics*, 2015; 35: 32-49.
- 35) Nakanishi M, Demura Y, Umeda Y, *et al*: Multi-arterial infusion chemotherapy for non-small cell lung carcinoma -significance of detecting feeding arteries and tumor staining. *Lung Cancer*, 2008; 61: 227-234.
- 36) Seki A, Hori S, Sueyoshi S, *et al*: Transcatheter arterial embolization with spherical embolic agent for pulmonary metastases from renal cell carcinoma. *Cardiovasc Intervent Radiol*, 2013; 36: 1527-1535.