Temporal variations in stump pressure and assessment of images obtained from cone-beam computed tomography during balloon-occluded transarterial chemoembolization

（B-TACE（Ballon-ocluded transarterial chemoembolization）における Stump pressure の経時変化と CBCT による画像評価）

申請者　弘前大学大学院医学研究科

総合医療・健康科学領域

放射線診断学教育研究分野

氏名　角田　晃久

指導教授　高井　良尋

Abstract

Aim: With balloon-occluded Transcatheter arterial chemoembolization (B-TACE), to show the optimized duration of balloon occlusion to start injection of lipiodol in order to maximize lipiodol deposition in the nodule, and to reveal the endpoint of lipiodol injection.

Methods: Of 29 consecutive patients who underwent balloon-occluded TACE between November 2013 and February 2014, we could measure stump pressure for 219 nodules in 27 patients. Tumors were counted, measured, and could be visually assessed in 20 of these patients at 26 sites. Tumors with multiple feeders were found in 8 patients. Arterial blood pressure was measured before, immediately after, and 5 minutes after balloon occlusion prior to intra-arterial injection, as well as before and after balloon deflation after intra-arterial injection. Images were assessed qualitatively by 2 radiologists as well as quantitatively by calculating the contrast-to-noise ratio.

Results: We found no significant difference in pressure between immediately after and 5 minutes after balloon occlusion. Mean stump pressure before balloon deflation after intra-arterial injection was 70.4 mmHg. We observed a significant increase in qualitative scores after balloon occlusion (P <0.001), and the mean score in the third-order branch was significantly higher than that in the first-order branch ($P = 0.048$).

Conclusion: Our results indicate that intra-arterial injection can be started at any time after balloon occlusion and that 70 mmHg may be considered as a possible indicator of the endpoint for arterial injection.

Introduction

Transarterial chemoembolization (TACE) contributes to improved prognosis for patients with hepatocellular carcinoma (HCC) for whom surgery or radiofrequency ablation is not indicated.[1,2] With TACE, it has been demonstrated that the more Lipiodol that accumulates in HCC, the lower is the local recurrence rate,[3] indicating the importance of improving accumulation of Lipiodol for TACE. In recent years, balloon-occluded TACE (B-TACE) using a microballoon catheter has been reported as a technique to enhance accumulation of Lipiodol in HCC. In this technique, balloon occlusion causes development of collateral circulation in the hepatic parenchyma, such as peribiliary plexus, [4] interlobar communicating arcade,[5] and isolated artery,[6] and the peripheral arterial circulation is preserved. Consequently, Stump pressure is reduced. Because the difference between stump and portal pressure becomes smaller, Lipiodol cannot pass through the arterioportal communication and therefore does not flow into the portal system. However, Lipiodol continues to flow into cancerous nodules where vascular resistance is low. In other words, the mechanism of this technique is assumed to enhance tumor selectivity by limiting flow into the normal hepatic parenchyma.[7,8] In this study, we attempted for the first time to measure stump pressure before and after balloon occlusion, as well as after intra-arterial injection, and to analyze temporal variations in stump pressure and influencing factors. Moreover, we visually and quantitatively assessed changes on cone-beam computed tomography (CBCT) images before and after balloon occlusion to determine the presence or absence, as well as the degree, of tumor selectivity.

Methods

Patients

This clinical study was approved by the ethics committees of our hospital and its affiliated hospitals. Of the patients who underwent B-TACE between November 2013 and February 2014, 29 consecutive patients with a total of 229 nodules provided informed consent. Of these patients, stump pressure could be examined for 219 nodules in 27 patients (15 men and 12 women), ranging in age from 42 to 88 (mean 68.3) years. Of these 27 patients, CBCT images could be assessed in 20 patients (26 sites). The patient characteristics are presented in Table 1.

Treatment protocol

For angiography devices, AXIOM Artis dBA (Siemens Healthcare ,Tokyo, Japan) and Innova IGS 630 (GE Healthcare ,Tokyo, Japan) were used. CBCT was used because there were no functions of the Angio-CT in the angiography devices that are used at this hospital. CBCT was performed before and after balloon occlusion prior to intra-arterial injection, as well as after TACE. We used a 4F Shepherd hook catheter and a long loop catheter for guiding catheters and 1.8F Attendant delta (TERUMO, Tokyo, Japan) and 1.8F LOGOS (PIOLAX, Kanagawa, Japan) for microballoon catheters. We used Lipiodol (iodized poppy seed oil fatty acid ester) at a mean dose of 4.1 (range 1–10) mL ($n = 33$), cisplatin at a mean dose of 32.6 (range 10–80) mg ($n = 23$), and epirubicin at a mean dose of 25.5 (range 15–45) mg ($n = 10$). We used cisplatin for a case in accord with the following conditions. (Less than 75 years old, More than eGFR 60mL/min, More than platelet 100×10^3/μl) epirubicin was used for the case which isn't relevant to this. 100mg of cisplatin or 50mg of epirubicin was combined with 5 mL of iohexol. The mixture of these solutions and 10 mL of Lipiodol was emulsified by vigorous pumping 20 times between two syringes that were interconnected with a three-way stopcock.

In principle, when the portal vein branches in the noncancerous area were visualized or when blood flow was arrested by injecting Lipiodol Emulsion (LE) intra-arterial injection was stopped, and embolization was performed with 1-mm

Gelpart (Nihonkayaku, Tokyo, Japan) particles. However, in patients with a large tumor or multiple tumors, embolization was performed with Gelpart particles while the portal vein branches remained unvisualized.

After the catheter was advanced as distally as possible, the artery was occluded with a balloon, and the drugs were injected. The occlusion sites were the first-order branch (level of the main trunks of the right and left hepatic arteries) in 10 sites, the second-order branch (level of a segmental branch) in 13 sites, and the third-order branch (level of a subsegmental branch or downstream) in 10 sites.

Tumors were counted on CBCT images as accurately as possible (range 1–58, median 1, mean 6.6 tumors). To determine tumor size, based on the Response Evaluation Criteria in Solid Tumors (RECIST[9]), the major axes of tumors were measured. In patients with multiple tumors, the length of the major axis of each tumor was added (range 10–486, median 25, mean 77 mm). In 8 patients, tumors with multiple feeders were found.

Blood pressure measurement

To measure blood pressure, the DTX Plus™ Disposable Blood Pressure Transducer (Argon Medical Devices, Tokyo, Japan) was used. After being connected to a catheter, the transducer shows pulse waves and measures blood pressure. To determine whether the device could measure blood pressure through the small lumen of a microballoon catheter, blood pressure was measured at the placement site of a guiding catheter by using the transducer passed through the guiding catheter and a microballoon catheter. Mean blood pressure values were used for analysis.

Arterial blood pressure was measured a total of 5 times, at the following time points, to examine variations in stump pressure: before, immediately after, and 5 minutes after balloon occlusion prior to intra-arterial injection, as well as before and after balloon deflation following intra-arterial injection.

Image assessment

For image assessment, 0.5-mm images were reconstructed to images with an average thickness of 3 mm.

Qualitative assessment

The contrast between tumors and the normal hepatic parenchyma around them was visually assessed by 2 radiologists (an interventional radiology specialist [14th year of practice] and a radiologist [fifth year]) and scored on a 4-point scale: 4, excellent; 3, good; 2, fair; and 1, poor.

Quantitative assessment

The CT value of CBCT is uneven than Multidetctor-raw CT (MDCT) and cannot just use it. Therefore the contrast-to-noise ratio (CNR) was calculated to perform quantitative assessment[10-12]. To minimize the effect of noise, regions of interest were set to be small (about $20mm^2$), and measurements were made at several points (at least 3 points) with a small standard deviation. Mean values were used to calculate CNR.

$$\mathrm{CNR} = \sqrt{\frac{Nt^2 - Nh^2}{Nh^2}}$$

Nt: tumor pixel values, Nh: surrounding hepatic parenchyma pixel values

Statistical analysis

The Shapiro-Wilk test was performed for each data set to examine the normality of data distribution. The data sets with normal distribution were assessed by Student's *t*-test, and those without normal distribution were assessed by Wilcoxon test. For comparisons among 3 groups or more, the Tukey-Kramer test was used. For qualitative assessment, κ values were used to verify the agreement in scoring between the examiners.

RESULTS

We observed a correlation between mean blood pressure measured with the guiding catheter and that measured with the microballoon catheter（P = 0.0001241 r = 0.797） (Figure 1). Prior to intra-arterial injection, mean blood pressure was 97 mmHg before balloon occlusion and 49.1 mmHg immediately after balloon occlusion, showing a significant decrease of 47.9 mmHg in arterial blood pressure (P<0.0001, Wilcoxon test). Mean blood pressure was 50.4 mmHg 5 minutes after balloon occlusion. No significant difference was observed in arterial blood pressure between immediately after and 5 minutes after balloon occlusion (P = 0.1243, Student's t-test). Before balloon deflation following intra-arterial injection, mean arterial blood pressure was 70.6 mmHg, showing a significant increase of 21.5 mmHg from the value immediately after balloon occlusion (P< 0.0001, Student's t-test). The mean arterial blood pressure after balloon deflation following intra-arterial injection was not significantly different from that before balloon occlusion (*P* = 0.9107, Student's *t*-test) (Figure 2).

In the assessment according to the occlusion sites, the mean stump pressure immediately after balloon occlusion was 49.7 mmHg in the first-order branch, 49.1 mmHg in the second-order branch, and 49.1 mmHg in the third-order branch, showing no significant difference ($P > 0.05$, Tukey-Kramer test). The percent changes between before and immediately after balloon occlusion were 49% overall, 47% in the first-order branch, 48% in the second-order branch, and 53% in the third-order branch. In addition, it has been reported that stump pressure is less than 64mmHg, there is assumed to enhance tumor selectivity[5]. The percentage that became less than 64mmHg were 73% overall, 67% in the first-order branch, 70% in the second-order branch, and 82% in the third-order branch. The mean stump pressure before balloon deflation was 74.1 mmHg in the first-order branch, 62.8 mmHg in the second-order branch, and 77.3 mmHg in the third-order branch, showing no significant difference ($P > 0.05$, Tukey-Kramer test). The percent changes between immediately after balloon occlusion prior to intra-arterial injection and before balloon deflation following intra-arterial injection were 30% overall, 32% in the first-order branch, 22% in the second-order branch, and 36% in the third-order branch.

The mean stump pressure immediately after balloon occlusion was 49.3 mmHg in cases with multiple feeders and 47 mmHg in cases without multiple feeders, showing no significant difference ($P = 0.922$, Student's t-test). The percent changes between before and immediately after balloon occlusion were 50% and 49%, respectively. The percentage that became less than 64mmHg were 70% in cases with multiple feeders and 77% in cases without multiple feeders. The mean pressure before balloon deflation was 72.6 mmHg in cases with multiple feeders and 68.3 mmHg in cases without multiple feeders, showing no significant difference ($P = 0.746$, Student's t-test). The percent changes compared with immediately after balloon occlusion were 31% and 30%, respectively (Tables 2,3). Although correlation with tumor size was evaluated, no clear correlation was observed between stump pressure and tumor size ($P = 0.7699$, $r = 0.07418264$) (Figure 3).

The mean stump pressure immediately after balloon occlusion was 47.5 mmHg in cases with cisplatin and 52.6 mmHg in cases with epirubicin, showing no significant difference ($P = 0.099$, Student's t-test).

Image assessment

Qualitative assessment

The mean scores before and after balloon occlusion were 2.1 and 3.0, respectively, showing a significant increase in the scores after balloon occlusion ($P < 0.001$, Wilcoxon test). After embolization, the mean score was 2.9 and not significantly different from that after balloon occlusion ($P = 0.63411$, Wilcoxon test). When the scores were compared among the first-order, second-order, and third-order branches, the mean scores were 2.3, 2.9, and 3.3, respectively, showing that the scores tended to be higher as the artery was occluded at more distal sites. The mean score in the third-order branch was significantly higher than that in the first-order branch ($P = 0.048$, Tukey-Kramer test) (Tables 6-8). Although the scores determined by Examiner A tended to be slightly higher, the κ values were high at 0.892 before balloon occlusion, 0.764 after balloon occlusion, and 0.822 after embolization (Tables 4,5).

Quantitative assessment

The contrast between tumors and the surrounding hepatic parenchyma was assessed with CNR. The mean CNR was 2.5 ± 1.6 (range 0.24–6.6) before balloon occlusion and 3.5 ± 2.0 (range 0.25–8.7) after balloon occlusion, a significant increase (P = 0.00014, Student's t-test). Although the mean CNR after embolization increased to 4.2 ± 2.7 (range 0.59–8.4), the increase was not significant (P = 0.31, Student's t-test).

The CNR after balloon occlusion was assessed according to the occlusion sites. The mean CNR in the first-order, second-order, and third-order branches was 2.7 ± 1.6, 3.5 ± 2.1, and 3.8 ± 2.1, respectively. A significant difference was observed between the first-order and second-order branches (P = 0.048, Student's t-test). No significant difference was observed either between the first-order and third-order branches or between the second-order and third-order branches (P = 0.121 and P = 0.931, respectively, Student's t-test).

The mean CNR after embolization in the first-order, second-order, and third-order branches was 2.1 ± 1.1, 4.4 ± 2.8, and 4.8 ± 2.8, respectively. Significant differences were observed both between the first-order and second-order branches and between the first-order and third-order branches (P = 0.025 and P = 0.042, respectively, Student's t-test). No significant difference was observed between the second-order and third-order branches (P = 0.802, Student's t-test).

The mean CNR after embolization in the above 70mmHg and under 70mmHg was 4.2±2.2 and 3.2±1.5, respectively. No significant difference was observed between the above 70mmHg and under 70mmHg($P = 0.204$, Student's t-test) (Table 6,7 and Figures 4a and 4b).

Discussion

It has already been reported that balloon occlusion improves tumor selectivity. In this study, because no significant difference was observed between immediately after and 5 minutes after balloon occlusion, it was assumed that balloon occlusion would instantly cause the development of collateral circulation, which would remain unchanged over time. Thus, it was assumed that there would not be any problem at whichever point after balloon occlusion intra-arterial injection was started. After intra-arterial injection, stump pressure increased, which is guessed that vascular resistance increases by performing embolization of tumor feeder. Moreover, as stump pressure increases, the difference between stump and portal pressure is increased. As a consequence, drugs also flow into the normal hepatic parenchyma, it was assumed that tumor selectivity would be reduced. There are also reports that dense LE accumulation in the HCC nodule could be achieved by B-TACE when BOASP was 64 mmHg or less[5]. From this, it was guessed that tumor feeder was embolization when stump pressure was more than 64mmHg. In addition, it has been demonstrated that the portal vein branches in the cancerous area were embolization, the lower is the local recurrence rate in HCC[13,14,15]. For the portal vein branches embolism, also continue the injection after tumor embolization. And stump pressure increases more. In this study, the mean stump pressure before balloon deflation after intra-arterial injection was 70.4 mmHg, Thus, the artery will be relatively well embolized if stump pressure before balloon deflation following intra-arterial injection is 70 mmHg or above, suggesting that this value might be a valid endpoint for intra-arterial injection.

After a balloon is deflated, arterial blood pressure becomes almost the same as the pressure before balloon occlusion. This is assumed to be attributable to the return of original blood flow due to balloon deflation. We consider it better to perform embolization using Gelpart after balloon deflation than during balloon occlusion. Because embolization using Gelpart is performed after intra-arterial injection, stump pressure is already elevated, and it was assumed that tumor selectivity would be reduced. Moreover, injection of Gelpart under balloon occlusion causes backward shift of the balloon[16], and increases the possibility of vascular injury; however, it seems that if embolization is performed after balloon deflation, vascular injury is unlikely to occur.

When stump pressure immediately after balloon occlusion was assessed according to the occlusion sites, no significant difference was observed among the first-order, second-order, and third-order branches. However, the percent change between before and after balloon occlusion tended to be slightly lower when the third-order branch was occluded compared with when the first-order or second-order branch was occluded. In addition, the percentage that is 64mmHg or less has tended to be high when the third-order branch was occluded compared with when the first-order or second-order branch was occluded. It seemed that as a catheter is advanced to a more distal section to occlude the artery, pressure might tend to decrease more. No significant difference in pressure before balloon deflation was observed at any occlusion site, and the percent change between immediately after balloon occlusion and before balloon deflation did not show any clear tendency, either.

According to the presence or absence of multiple feeders, no significant difference in stump pressure was observed between before and immediately after balloon occlusion and between immediately after balloon occlusion and before balloon deflation. This might be attributable to the small number of cases with multiple feeders. However, the percentage that is 64mmHg or less has tended to be higher the cases without multiple feeders than the cases with multiple feeders. It seemed that without multiple feeders, stump pressure might tend to decrease more.

According to tumor size, no clear correlation was observed. This might be attributable to the facts that the tumor size did not vary much and the majority of the samples were distributed in a certain size range.

According to visual assessment, the scores after balloon occlusion were significantly higher than those before balloon occlusion, suggesting that balloon occlusion improved tumor selectivity. No significant difference was observed between after balloon occlusion and after embolization. Between the examiners, the scores determined by Examiner A were slightly higher overall, which might have been affected by differences in experience. However, the κ values indicated excellent agreement in any score before and after balloon occlusion as well as after embolization.

According to the quantitative assessment, CNR after balloon occlusion was also higher than that before balloon occlusion, suggesting that balloon occlusion improved tumor selectivity. CNR after embolization tended to be higher than that after balloon occlusion, likely because the dose of contrast media used for imaging after balloon occlusion was smaller, whereas an adequate dose of Lipiodol was intra-arterially injected after embolization; thus, CNR might have increased. In assessment according to the occlusion sites, the scores and CNR for the second-order and third-order branches were significantly higher than those for the first-order branch, suggesting that tumor selectivity might be improved if a catheter is advanced to a more distal section to occlude the artery. No significant difference in CNR after embolization was observed between above 70mmHg and under 70mmHg. However, CNR has tended to be higher above 70mmHg than under 70mmHg. It seemed that above 70mmHg, lipiodol accumulation might tend to become dense more. From this, it is suggested that above 70mmHg may become the endpoint of the intra-arterial injection.

It has been reported that iodine-131 (I-131) lipiodol ultra fluid injected into the hepatic artery concentrated in the HCC with a tumorous (T) to nontumorous (NT) activity ratio (T/NT) of 4.3 ± 3.6 [17]. If the I-131 T/NT ratio was comparable with the CNR, the mean CNR in the second-order and third-order branches was 4.4 ± 2.8 and 4.8 ± 2.8 , B-TACE might improve I-131 T/NT ratio. We consider improved LE accumulation by B-TACE could also be applied to improve the effect of radioembolization with I-131 lipiodol ultra fluid for the treatment of HCC[18,19]. Our study has limitations that is assumed that no significant difference might have been observed in assessment according to the presence or absence of multiple feeders due to the small sample size. Moreover, the small sample size prevented us from examining tumor sites. We would like to conduct studies on these aspects in the future.

Conclusion

Balloon occlusion was suggested to reduce arterial blood pressure and to improve tumor selectivity. There seemed to be no problem at whichever point after balloon occlusion intra-arterial injection was started. After intra-arterial injection, arterial blood pressure increased up to approximately 70 mmHg, which was suggested as a possible indicator of the endpoint for arterial injection.

References

1） Llovet JM, Bruix J. Systematic review of randomized trials for unresectable hepatocellular carcinoma: chemoembolization improves survival. Hepatology 2003;37:429-442

2） Lo CM, Ngan H, Tso WK et al.Randomized controlled trial of transarterial lipiodol chemoembolization for unresectable hepatocellular carcinoma. Hepatology 2002;35:1164-1171

3） 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

4） Cho KJ, Lunderquist A.The peribiliary vascular plexus:the microvascular architecture of the bile duct in the rabbit and inclinical cases. Radiology 1983;147:357-364

5） Tohma T, Cho A, Okazumi S et al.Communicating arcade between the right and left hepatic arteries: evaluation with CT and angiography during temporary balloon occlusion of the right or left hepatic artery. Radiology 2005;237:361-365

6） Ekataksin W .The isolated artery: an intrahepatic arterial pathway that can bypass the lobular parenchyma in mammalian livers. Hepatology 2000;31:269-279

7) Irie T, Kuramochi M, Takahashi N.Improved accumulation of lipiodol under balloon-occluded transarterial chemoembolization (B-TACE) for hepatocellular carcinoma: measurement of blood pressure at the embolized artery before and after balloon inflation. IVR 2011;26:49-54

8) Irie T, Kuramochi M, Takahashi N.Dense Accumulation of Lipiodol Emulsion in Hepatocellular Carcinoma Nodule during Selective Balloon-occluded Transarterial Chemoembolization: Measurement of Balloonoccluded Arterial Stump Pressure. Cardiovasc Intervent Radiol 2013;3:706-713

9) E.A. Eisenhauera, P. Therasseb, J. Bogaertsc et al.New response evaluation criteria in solid tumours:Revised RECIST guideline (version 1.1) EUROPEAN JOURNAL OF CANCER 2009;45:228-247

10) Kanda M, Kanbayashi T, Mathuzaki H et al.Comparison of CT number of medical CT and pixel value of dental cone beam CT. The Journal of the Japanese Society for Dental Materials and Devices 2013;32(1):41-51

11) Mikami I, Kuroe T, Taniyama T et al.Evaluation of Pixel Value of Dental Cone beam CT. Journal of Japanese Society of Oral Implantology 2011;24(3):405-413

12) Mizuno Y, Doi T, Kokubo K et al.Evaluation of Low Contrast Resolution Using

Contrast-to-noise Ratio in CT. Radiological Physics and Technology 1999;55(8):778-782

13) Demachi H, Matsui O, Abo H et al.Simulation model based on non-Newtonian fluid mechanics applied to the evaluation of the embolic effect of emulsions of iodized oil and anticancer drug. Cardiovascular Interventinal Radiology 2000;23:285-290

14) Anai H, Tanaka T, Nishiofuku H et al.Conventional TACE:Transcatheter Arterial Chemo-Embolization. IVR 2013;28:418-426

15) Irie T, Kuramochi M, Takahashi N.Balloon-occluded Trans - Arterial Chemoembolization (B - TACE) : Comparison with Ultra – selective TACE (U – TACE) IVR 2013;28:436-442

16) Irie T, Kuramochi M, Ishikawa A.Safety of Balloon-Occluded Transarterial Chemoembolization (B-TACE) for Hepatocellular Carcinoma : Analysis of Adverse Events in 82 Cases. IVR 2011;26:175-181

17) Raoul JL, Bourguet P, Bretagne JF et al. Hepatic artery injection of I-131-labeled lipiodol. Part I. Biodistribution study results in patients with hepatocellular carcinoma and liver metastases. Radiology 1988;168:541-545

18) Lau WY, Lai ECH, Leung TWT et al. Adjuvant intraarterial iodine-131-labeled

lipiodol for resectable hepatocellular carcinoma: a prospective randomized trial–update on 5-year and 10-year survival. Ann Surg 2008;247:43-48

19）Chua TC, Chu F, Butler SP et al.Intra-arterial iodine-131- lipiodol for unresectable hepatocellular carcinoma. Cancer 2010;116:4069-4077

Figure 1 The guiding catheter and the microballoon catheter correlation

Good correlation was obtained between mean blood pressure measured with the guiding catheter and that measured with the microballoon catheter. (P = 0.0001241 r = 0.797)

Figure 2 Temporal variations in stump pressure

The mean blood pressure was 97 mmHg before balloon occlusion and 49.1 mmHg immediately after balloon occlusion (P <0.0001, Wilcoxon test). Mean blood pressure was 50.4 mmHg 5 minutes after balloon occlusion. No significant difference was observed in arterial blood pressure between immediately after and 5 minutes after balloon occlusion (P = 0.1243, Student's t-test). Before balloon deflation, mean arterial blood pressure was 70.6 mmHg (P < 0.0001, Student's t-test). The mean arterial blood pressure after balloon deflation was not significantly different from that before balloon occlusion (P = 0.9107, Student's t-test).

Figure 3 Stump pressure and tumor size correlation

No clear correlation was observed between stump pressure and tumor size (P = 0.7699, r＝0.07418264).

Figure 4a CNR measurement (before occlusion)

CBCT obtained before balloon occlusion revealed LE accumulation in HCC and liver parenchyma of the embolized region.

Figure 4b CNR measurement(after occlusion)

CBCT obtained after balloon occlusion revealed LE accumulation in HCC and liver parenchyma of the embolized region.

Table 1 Patient characteristics

Characteristic	Value
Gender（M：F）	15：12
Age（y）	Mean 68.3 （Range 42-88）
HCC （primary：Recurrence）	10：17
Virus（Hepatitis B：C：non-B,non-C）	3：15：9
Child-Pugh（A：B）	17：10
Diameter of HCC（mm）	Mean 76.5 （Range 10-486）

Abbreviations: HCC, hepatocellular carcinoma; F, female; M, male.

Table 2 Blood pressure immediately after balloon occlusion and percent change between before and after balloon occlusion

	Immediately after balloon occlusion: Mean pressure (mmHg)	Percent change between before and after balloon occlusion (%)	The percentage that became less than 64mmHg (%)
All cases	49.3	49%	73%
1st-order branch	49.7	47%	67%
2nd-order branch	49.1	48%	70%
3rd-order branch	49.1	53%	82%
Multifeeder（+）	49.3	50%	70%
Multifeeder（－）	47	49%	77%

Percent change was calculated as [(pressure before balloon occlusion - pressure immediately after occlusion)/(before balloon occlusion)] × 100.

Table 3 Blood pressure before balloon deflation following intra-arterial injection and percent change between immediately after balloon occlusion and before balloon deflation

	Before balloon deflation following intra-arterial injection ：Mean pressure (mmHg)	Percent change between immediately after balloon occlusion and before balloon deflation (%)
All cases	70.6	30%
1st-order branch	74.1	32%
2nd-order branch	62.8	22%
3rd-order branch	77.3	36%
Multifeeder（＋）	72.6	32%
Multifeeder（－）	68.3	31%

Percent change was calculated as [(pressure before balloon deflation - pressure immediately after balloon deflation)/(before balloon occlusion)] × 100.

Table 4 Qualitative assessment : all cases and the occlusion sites

	Before occlusion	After occlusion	After embolization
Examiner A	2.0	3.1	2.9
Examiner B	2.2	2.9	2.8
Overall	2.1	3.0	2.9
	First-order branch	Second-order branch	Third-order branch
Examiner A	2.2	3.1	3.4
Examiner B	2.5	2.7	3.2
Overall	2.3	2.9	3.3

The mean scores before and after balloon occlusion were 2.1 and 3.0, respectively, showing a significant increase in the scores after balloon occlusion ($P < 0.0001$, Wilcoxon test). After embolization, the mean score was 2.9 and not significantly different from that after balloon occlusion ($P = 0.63411$, Wilcoxon test).

When the scores were compared among the first-order, second-order, and third-order branches, the mean scores were 2.3, 2.9, and 3.3, respectively, showing that the scores tended to be higher as the artery was occluded at more distal sites. The mean score in the third-order branch was significantly higher than that in the first-order branch (P = 0.048, Tukey-Kramer test)..

Table 5 Qualitative assessment: agreement between examiners

	κ values
Before occlusion	0.892
After occlusion	0.764
After embolization	0.822

The κ values were high at 0.892 before balloon occlusion, 0.764 after balloon occlusion, and 0.822 after embolization, Reproducibility of the A and B were very excellent.

Table 6 Quantitative assessment (all cases) : contrast-to-noise ratio

	Mean	Range
Before balloon occlusion	2.5±1.6	0.24-6.6
After balloon occlusion	3.5±2.0	0.25-8.7
After embolization	4.2±2.7	0.59-9.5

The contrast between tumors and the surrounding hepatic parenchyma was assessed with CNR. The mean CNR was 2.5 ± 1.6 (range 0.24–6.6) before balloon occlusion and 3.5 ± 2.0 (range 0.25–8.7) after balloon occlusion, a significant increase ($P < 0.0001$, Student's t-test). Although the mean CNR after embolization increased to 4.2 ± 2.7 (range 0.59–8.4), the increase was not significant ($P = 0.31$, Student's t-test).

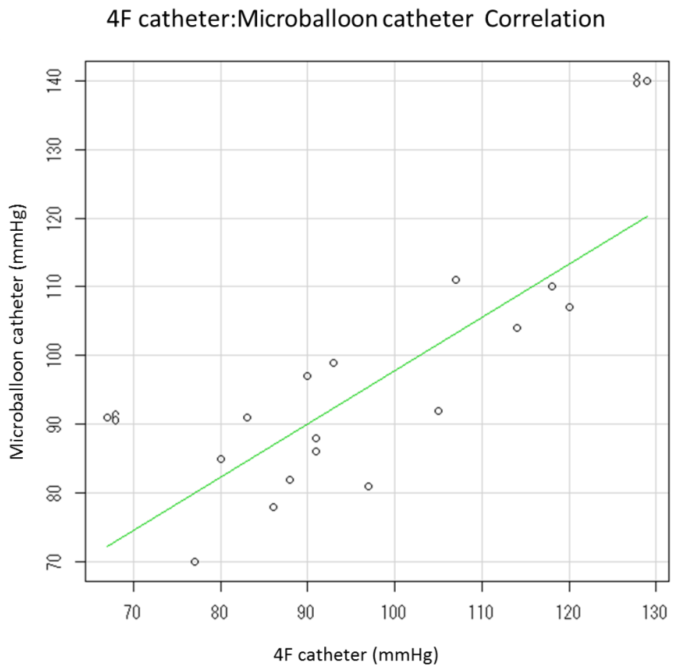
Table 7 Quantitative assessment (the occlusion sites) : contrast-to-noise ratio

After balloon occlusion	
First-order branch after occlusion	2.7±1.6
Second-order branch after occlusion	3.5±2.1
Third-order branch after occlusion	3.8±2.1
After embolization	
First-order branch after embolization	2.1±1.1
Second-order branch after embolization	4.4±2.8
Third-order branch after embolization	4.8±2.8
Above 70mmHg	4.2±2.2
Under 70mmHg	3.2±1.5

After balloon occlusion , A significant difference was observed between the first-order and second-order branches (P = 0.048, Student's t-test). No significant difference was observed either between the first-order and third-order branches or between the second-order and third-order branches (P= 0.121 and P = 0.931, respectively, Student's t-test).

After embolization , Significant differences were observed both between the first-order and second-order branches and between the first-order and third-order branches (P = 0.025 and P = 0.042, respectively, Student's t-test). No significant difference was observed between the second-order and third-order branches (P = 0.802, Student's t-test). No significant difference was observed between above 70mmHg and under 70mmHg. (P = 0.204, Student's t-test)

Figure 1 The guiding catheter and the microballoon catheter correlation



$y = 0.7747x + 20.265$

$R^2 = 0.6366$

Figure 2 Temporal variations in stump pressure

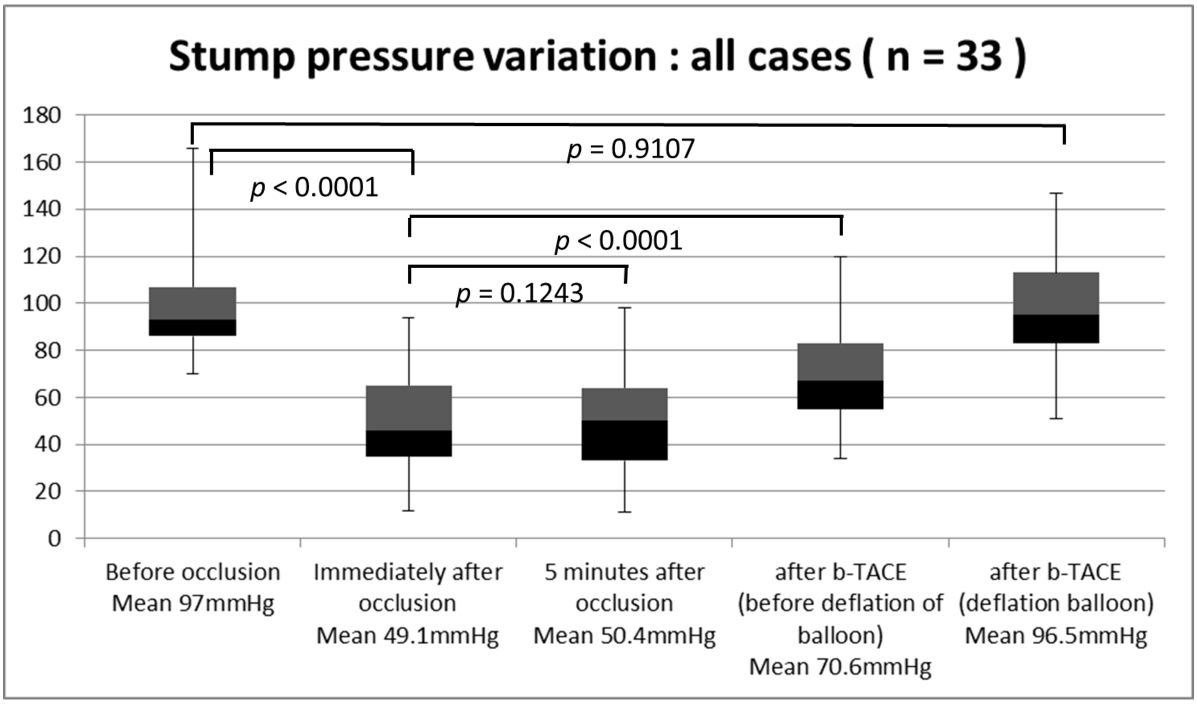


Figure 3 Stump pressure and tumor size correlation

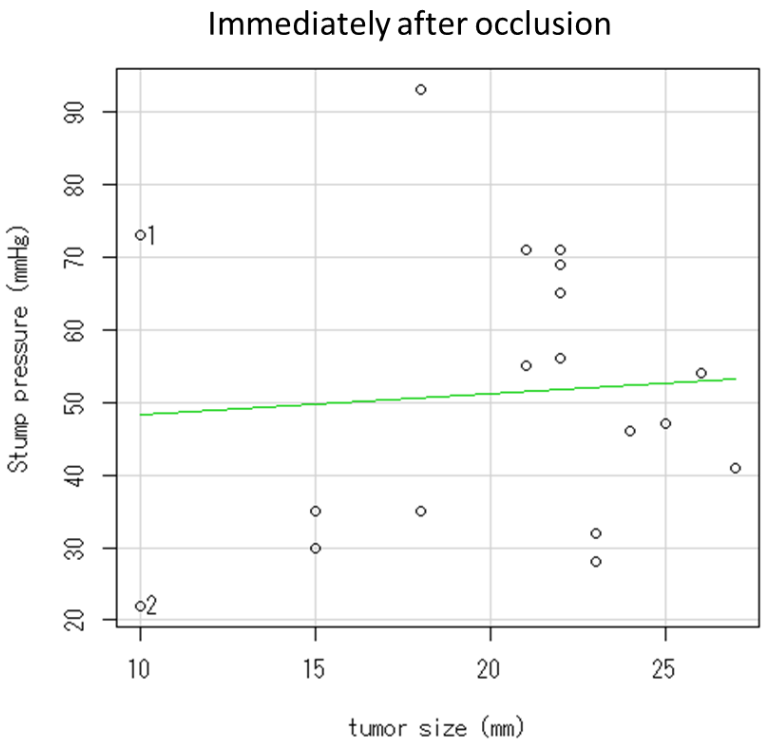


Figure 4a CNR measurement (before occlusion)

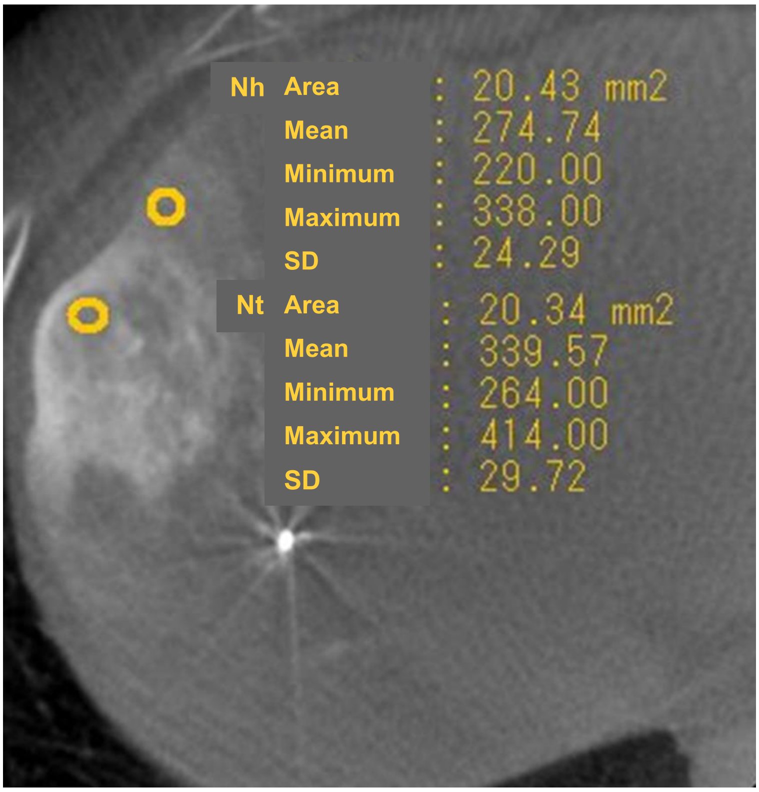


Figure 4b CNR measurement(after occlusion)