

## Segmental transarterial chemoembolization with Lipiodol mixed with anticancer drugs for nonresectable hepatocellular carcinoma: follow-up CT and therapeutic results

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**Abstract.** We developed segmental Lp-TAE, which is transcatheter hepatic sub-subsegmental, subsegmental, or segmental chemoembolization using Lipiodol introduced into the tumor-bearing hepatic sub-subsegment, subsegment, or segment as the target area. A total of 98 patients with nonresectable hepatocellular carcinoma (HCC) undergoing segmental Lp-TAE (Seg-Lp-TAE) were studied, and the relationship between the CT pattern observed after Seg-Lp-TAE (Seg-Lp-CT) and the therapeutic results obtained in those patients was evaluated. Seg-Lp-CT was classified into four types (type I, homogeneous; type II, defective; type III, inhomogeneous; and type IV, only slight accumulation, if any) according to the Lipiodol accumulation pattern observed after Seg-Lp-TAE. The cumulative nonrecurrence rates of type I were higher than those of types II–IV. The cumulative survival rates of type Ia, in which Lp accumulation is also seen around the main tumor, were the highest (93.8% at 1 year, 85.9% at 2 years, 85.9% at 3 years, and 57.3% at 4 years). The cumulative survival rates achieved with Seg-Lp-TAE were 89.2% at 1 year, 69.4% at 2 years, 58.9% at 3 years, 44.0% at 4 years, and 30.2% at 5 years, which were higher than those achieved with conventional Lp-TAE. Seg-Lp-TAE is very useful in the treatment of HCC limited to one sub-subsegment, subsegment, or segment, and it is important to choose sub-subsegmental, subsegmental, or segmental Lp-TAE on the basis of the size and site of the tumor as well as the type and the number of feeding arteries.

### Introduction

The role of transcatheter hepatic arterial chemoembolization (TAE) in the treatment of hepatocellular carcinoma (HCC) has been largely established, although much research is in progress to enhance the therapeutic results further by improving the embolization methods and developing better embolic materials [1, 5, 6, 10, 12–15, 17, 20, 22]. In recent years, to achieve more prolonged intratumor retention of anticancer agents and enhance the embolization effect, chemoembolization using an oily contrast medium (Lipiodol, Lp) mixed with an anticancer agent followed by the injection of gelatin sponge (GS) particles (Lp-TAE) has come to be widely performed [5, 6, 12–15, 17, 20]. We obtained relatively good results in 863 cases of nonresectable HCC in which Lp-TAE was performed, but they were not entirely satisfactory because of the deterioration in liver function induced by embolization of the entire liver, especially in cases with hepatic dysfunction, and the high incidence of local recurrence within 6 months. To enhance further the antitumor effect and reduce the adverse effects on the surrounding nontumorous tissues, we developed segmental Lp-TAE (Seg-Lp-TAE), which is transcatheter hepatic sub-subsegmental or segmental chemoembolization using Lp-TAE introduced into the tumor-bearing hepatic subsegment or segment as the target area [8, 9, 16, 18, 21]. In the present report, we describe the relationship between the CT patterns observed after Seg-Lp-TAE (Seg-Lp-CT) and the therapeutic results obtained in non-resectable HCC cases.

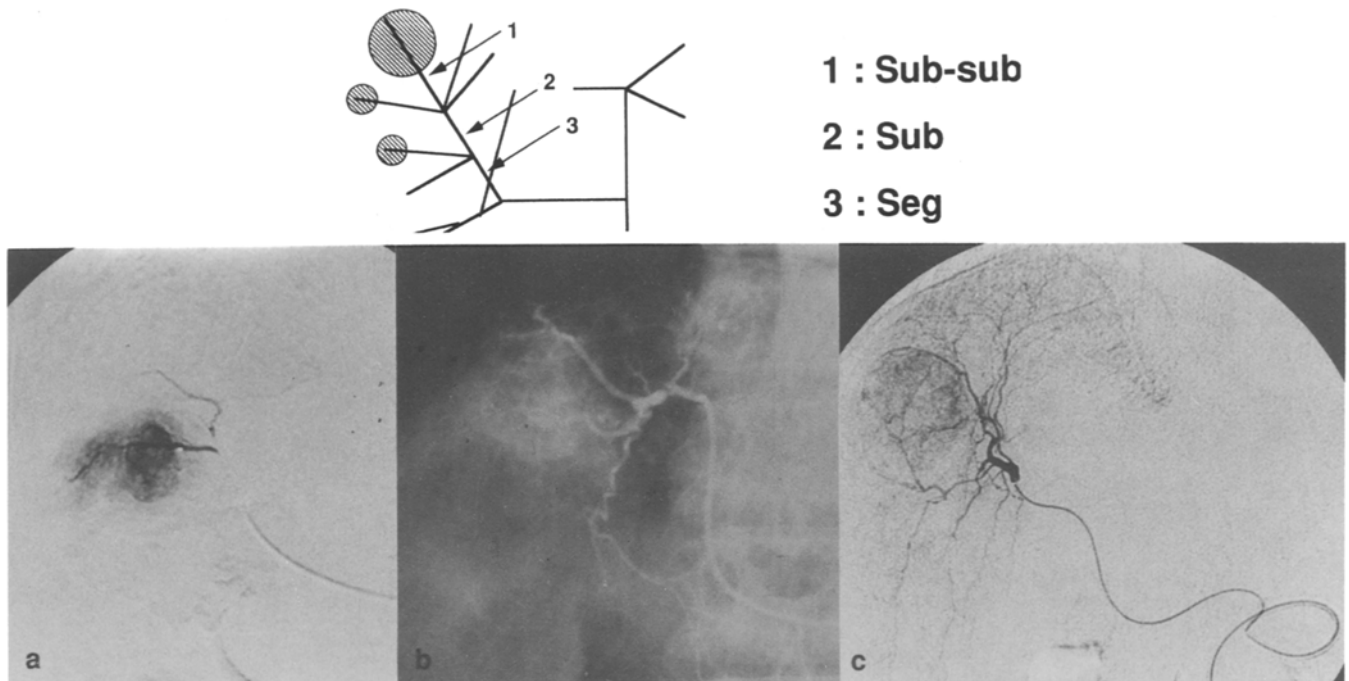
### Materials and methods

#### 1. Method of Seg-Lp-TAE

Superselective catheterization of the artery or arterial branch supplying the cancer-bearing segment (Seg), subsegment (Sub), or sub-subsegment (Sub-sub) was performed using in most cases a 5.5-F-long, tapered catheter with a 4.5-F tip (Cook Co.), although recently coaxial catheter systems such as Tracker 18 infusion catheters (Target Ther-

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**Fig. 1.** Definition of Seg-Lp-TAE. Seg-Lp-TAE: Superselctive hepatic arterial chemoembolization therapy by infusing Lipiodol mixed with an anticancer agent only to the cancer-bearing hepatic sub-subsegment (1, *Sub-sub*), subsegment (2, *Sub*), or segment (3, *Seg*).

apeutics Inc.) have also been employed (Fig. 1). Anticancer drugs mixed with Lp were infused into the cancer-bearing segment, subsegment, or sub-subsegment, and then TAE was performed with GS particles. Figure 1 defines Seg-Lp-TAE by use of a schematic drawing and an example.

We determined the volume of Lp (D ml) in proportion to the tumor diameter (d cm) and vascularity. The value obtained for the volume of Lp (D) was almost the same as that determined for the tumor diameter (d):  $D = d$ . The volume of Lp to be used was 1–10 ml (mean, 4.5 ml), which was determined by the size of the tumor, the area to be embolized, and the liver function. The anticancer drugs were dissolved in a solution of water-soluble contrast medium and distilled water, adjusted to a specific gravity equal to that of Lp, and then mixed with twice the volume of Lp to make an emulsion by the pumping method (20 times). As the anticancer drug Adriamycin (10–60 mg; mean, 35.5 mg) was mainly used alone or in combination with mitomycin C (5–20 mg; mean, 9.4 mg) or cisplatin (25–50 mg; mean, 42.5 mg), with the doses being adjusted according to the size of the tumor, the number of subsegments to be embolized, and the liver function.

## 2. Materials

A total of 98 patients with nonresectable HCC undergoing Seg-Lp-TAE were studied. Prior to this procedure, the main tumor was demonstrated by high-quality diagnostic imaging to be limited to one segment, subsegment, or sub-subsegment, with any daughter nodules being located in the same segment as the main tumor. In all cases, not only segmental resection but also tumor enucleation were contraindicated due to hepatic dysfunction, old age, or patient refusal. There were 73 men and 25 women ranging in age from 37–85 years (mean, 61.2 years), who were followed for more than 6 months after Seg-Lp-TAE.

The main tumor measured 1.5–10.5 cm (mean, 3.8 cm). There were 93 cases of the nodular type (36 cases, <3 cm in diameter; 37 cases, 3–5 cm; 19 cases, 5–10 cm; 1 case, >10 cm) and 5 cases of the massive type. Following the nomenclature of Couinaud [3], the main

(a) Sub-subsegmental arteriogram of the ventral branch of subsegmental artery supplying S5 (example of Sub-sub). (b) Subsegmental arteriogram of S4 (example of Sub). (c) Segmental arteriogram of right anterior segment (S8 and S5, example of Seg)

**Table 1.** Relationship between tumor type and embolized site of HCC treated by Seg-Lp-TAE

	Nodular (cm)				Massive	Totals
	0–3	3–5	5–10	>10		
Sub-sub	4	2	1			7
Sub	16	13	8		1	38
Seg	16	22	10	1	4	53
Total	36	37	19	1	5	98

tumor was located in segment 2 (S2) in 4 cases, in S3 in 11 cases, in S4 in 10 cases, in S5 in 11 cases, in S6 in 15 cases, in S7 in 7 cases, and in S8 in 40 cases. Daughter nodules were present in 21 of the cases, and they were localized in the same segment as the main tumor. Child's classification showed 53 cases of Child's A, 40 cases of Child's B, and 15 cases of Child's C. A Sub-sub was embolized in 7 cases; a Sub, in 38 cases; and a Seg, in 53 cases. Table 1 shows the relationship between the tumor type and the embolized site. The therapeutic results obtained in 863 cases treated by conventional Lp-TAE were used for comparison with the Seg-Lp-TAE cases [12].

## 3. Follow-up examination after Seg-Lp-TAE

Measurement of  $\alpha$ -fetoprotein (AFP) and CT examination combined with dynamic CT were performed before the procedure, after 1–2 weeks and 4 weeks, and at 3-month intervals thereafter. MRI was also used for selected cases when indicated. DSA was carried out when recurrence was suspected due to elevation of AFP and/or Seg-Lp-CT. Even when no recurrence was recognized by Seg-Lp-CT, AFP, or MRI, CTAP and DSA were performed at 1-year intervals to detect recurrence as early as possible.

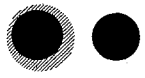



Type I	Type II	Type III	Type IV
a      b			
			
Homogeneous	Defective	Inhomogeneous	No/slight Accumulation

Fig. 2. Lipiodol accumulation patterns observed on CT scans after Seg-Lp-TAE for HCC

#### 4. Analytical methods

i) *Classification of Seg-Lp-CT after Seg-Lp-TAE.* Seg-Lp-CT was classified according to the pattern of Lp accumulation after Seg-Lp-TAE (Fig. 2):

1. Type I – the main tumor shows homogeneous Lp accumulation.
2. Type Ia – Lp accumulation is also seen around the main tumor.
3. Type Ib – Lp accumulation is not seen around the main tumor.
4. Type II – defects are found in Lp accumulation in the main tumor.
5. Type III – inhomogeneous Lp accumulation is seen in the main tumor.
6. Type IV – Only slight Lp accumulation, if any, is observed in the main tumor.

ii) *Criteria of recurrence.* Recurrence was judged on the basis of both the AFP data and diagnostic images. Elevation of AFP is an important sign of recurrence, but it is absent in some recurrent cases. Thus, diagnostic images are indispensable. Judgment of recurrence from images was mainly performed using CT, dynamic CT, and DSA images. When a tumor stain was recognized in a defective or non-accumulation area in cases of type II, III, or IV and at part of the circumference of Lp accumulation in type I, we judged the tumor to be recurrent. Cumulative survival rates were calculated by the Kaplan-Meier method.

iii) *Analyzed items.* The following items were analyzed:

1. The incidence of each CT pattern of Lp accumulation at 4 weeks after Seg-Lp-TAE
2. The incidence of recurrence for each CT pattern at 4 weeks after Seg-Lp-TAE
3. A comparison of cumulative nonrecurrence rates on the basis of Seg-Lp-CT after 4 weeks
4. A comparison of cumulative survival rates on the basis of Seg-Lp-CT after 4 weeks
5. A comparison of the cumulative survival rates achieved with Seg-Lp-TAE and conventional Lp-TAE
6. A comparison of cumulative survival rates as a function of the tumor type
7. A comparison of cumulative survival rates as a function of the embolized site
8. The relationships between Seg-Lp-CT, tumor type, and embolized site

## Results

### 1. Incidence of each CT pattern of Lp accumulation at 4 weeks after Seg-Lp-TAE

We analyzed the Seg-Lp-CT at 4 weeks after Seg-Lp-TAE for 67 cases. There were 18 cases of type Ia (Fig. 3), 29 cases of type Ib, 19 cases of type II (Fig. 4), and 1 case of type IV, whereas there was no case of type III. Among these

67 cases, we could analyze the Seg-Lp-CT at 2 weeks after Seg-Lp-TAE for 56 cases. There were 38 cases of type Ia, 4 cases of type Ib, 13 cases of type II, and 1 case of type IV. Of the 38 type Ia cases evaluated at 2 weeks after Seg-Lp-TAE, 18 continued to show type Ia, 18 showed type Ib, and 2 showed type II at 4 weeks after Seg-Lp-TAE. Of the 4 type Ib cases evaluated at 2 weeks after Seg-Lp-TAE, 3 continued to show type Ib and 1 showed type II at 4 weeks after Seg-Lp-TAE. All cases of type II or IV analyzed at 2 weeks remained the same type at 4 weeks after Seg-Lp-TAE. Accordingly, the incidence of type Ia decreased from 38/56 (76%) at 2 weeks to 18/67 (27%) at 4 weeks, whereas that of type Ib increased from 4/56 (7%) to 29/67 (43%) and that of type II increased from 13/56 (23%) to 19/67 (28%).

### 2. Incidence of recurrence for each CT pattern at 4 weeks after Seg-Lp-TAE

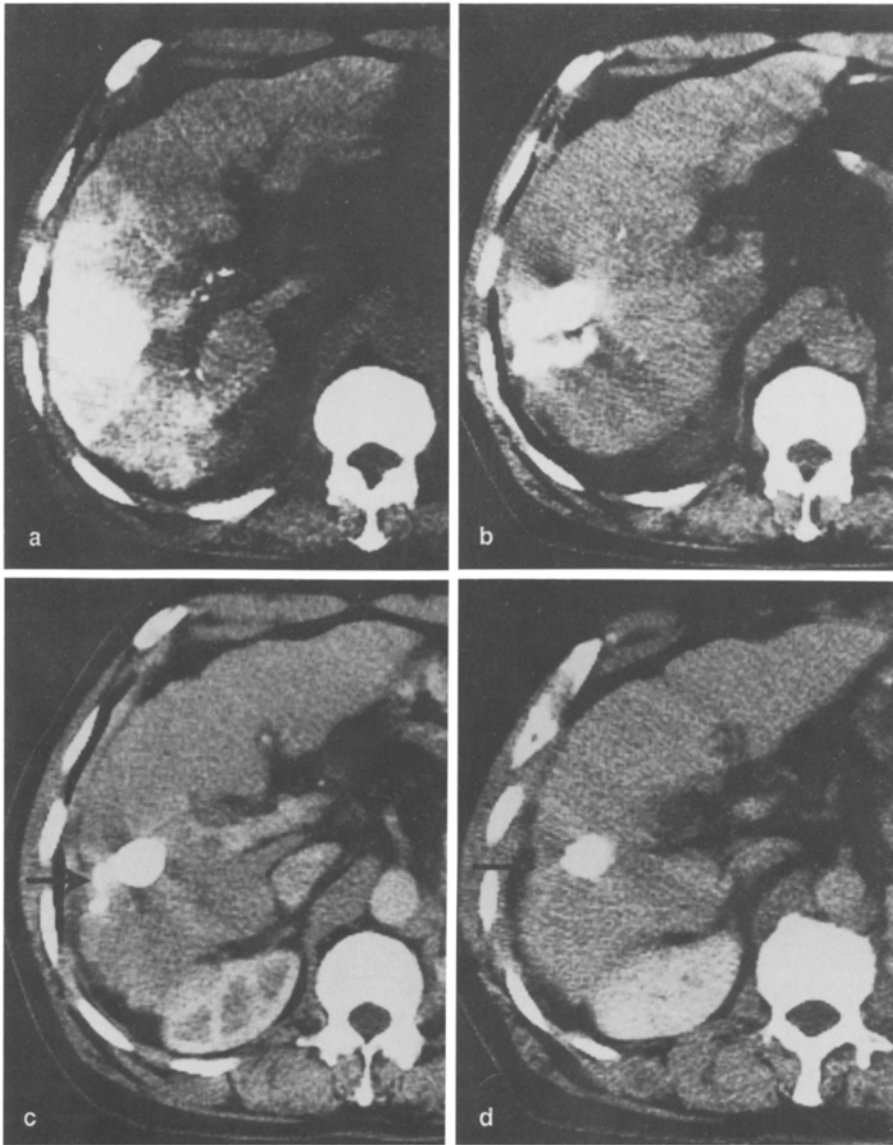
Recurrence of the main tumor during the subsequent follow-up was found in 30 of the 67 cases in which Seg-Lp-CT after 4 weeks could be analyzed (44.8%). These comprised 7 of the 18 type Ia cases (38.9%), 11 of the 29 type Ib cases (37.9%), 11 of the 19 type II cases (57.9%) (Fig. 4), and the 1 type IV case (100%). Seg-Lp-CT at the time of recurrence showed type Ia in no case, type Ib in 6 cases (Seg-Lp-CT after 4 weeks: type Ia in 2 cases, type Ib in 4 cases), type II in 12 cases (type Ia in 3 cases, type Ib in 4 cases, and type II in 5 cases), type III in 10 cases (type Ia in 2 cases, type Ib in 2 cases, and type II in 6 cases), and type IV in 2 cases (type Ib and type IV in 1 case each). In 20 of the 30 cases (66.7%), the degree of Lp accumulation was decreased on the Seg-Lp-CT obtained at the time when recurrence was diagnosed as compared with the Seg-Lp-CT obtained at 4 weeks after Seg-Lp-TAE, whereas in 10 cases (33.3%) the same type of Seg-Lp-CT pattern was seen.

### 3. Comparison of cumulative nonrecurrence rates on the basis of Seg-Lp-CT after 4 weeks (Fig. 5)

The cumulative nonrecurrence rates of type I (type Ia: 87.4% at 1 year, 65.5% at 2 years, 57.4% at 3 years, and 43.0% at 4 years; type Ib: 81.0%, 65.8%, 45.1%, and 45.1%, respectively) were higher than the rates of type II (48.7%, 19.5%, 0, and 0, respectively).

### 4. Comparison of cumulative survival rates on the basis of Seg-Lp-CT after 4 weeks (Fig. 6)

The cumulative survival rates of type Ia were the highest, being 93.8% at 1 year, 85.9% at 2 years, 85.9% at 3 years, and 57.3% at 4 years, with the corresponding figures for type Ib being 88.1%, 70.7%, 58.7%, and 44.1% and those for type II being 88.8%, 65.6%, 52.5%, and 35.0%.



**Fig. 3.** A 54-year-old man who underwent Seg-Lp-TAE for HCC in S5. CT scans obtained at 1 week after (a), 4 weeks after (b), and 6 months after the procedure (c) showed type Ia, and a CT scan obtained at 3 years after Seg-Lp-TAE (d) showed type Ib. The tumor was observed to diminish in size during the follow-up period. The tumor-bearing embolized segment showed atrophic change ( ) with time. This patient survived for more than 3 years

##### 5. Comparison of cumulative survival rates achieved with Seg-Lp-TAE and conventional Lp-TAE

The cumulative survival rates achieved with Seg-Lp-TAE (89.2% at 1 year, 69.4% at 2 years, 58.9% at 3 years, 44.0% at 4 years, and 30.2% at 5 years) were higher than those achieved with conventional Lp-TAE (60.7%, 37.7%, 22.4%, 14.5%, and 7.1%, respectively). Also, in the nodular type measuring less than 5 cm, the cumulative survival rates achieved with Seg-Lp-TAE (93.3%, 74.7%, 63.1%, 43.7%, and 32.8%, respectively) were higher than those achieved with conventional Lp-TAE (78.8%, 51.6%, 35.5%, 28.1%, and 15.2%, respectively).

##### 6. Comparison of cumulative survival rates as a function of the tumor type

The cumulative survival rates of the nodular type measuring less than 3 cm in diameter were the highest being 100% at 1 year, 85.4% at 2 years, 73.1% at 3 years, and 73.1% at

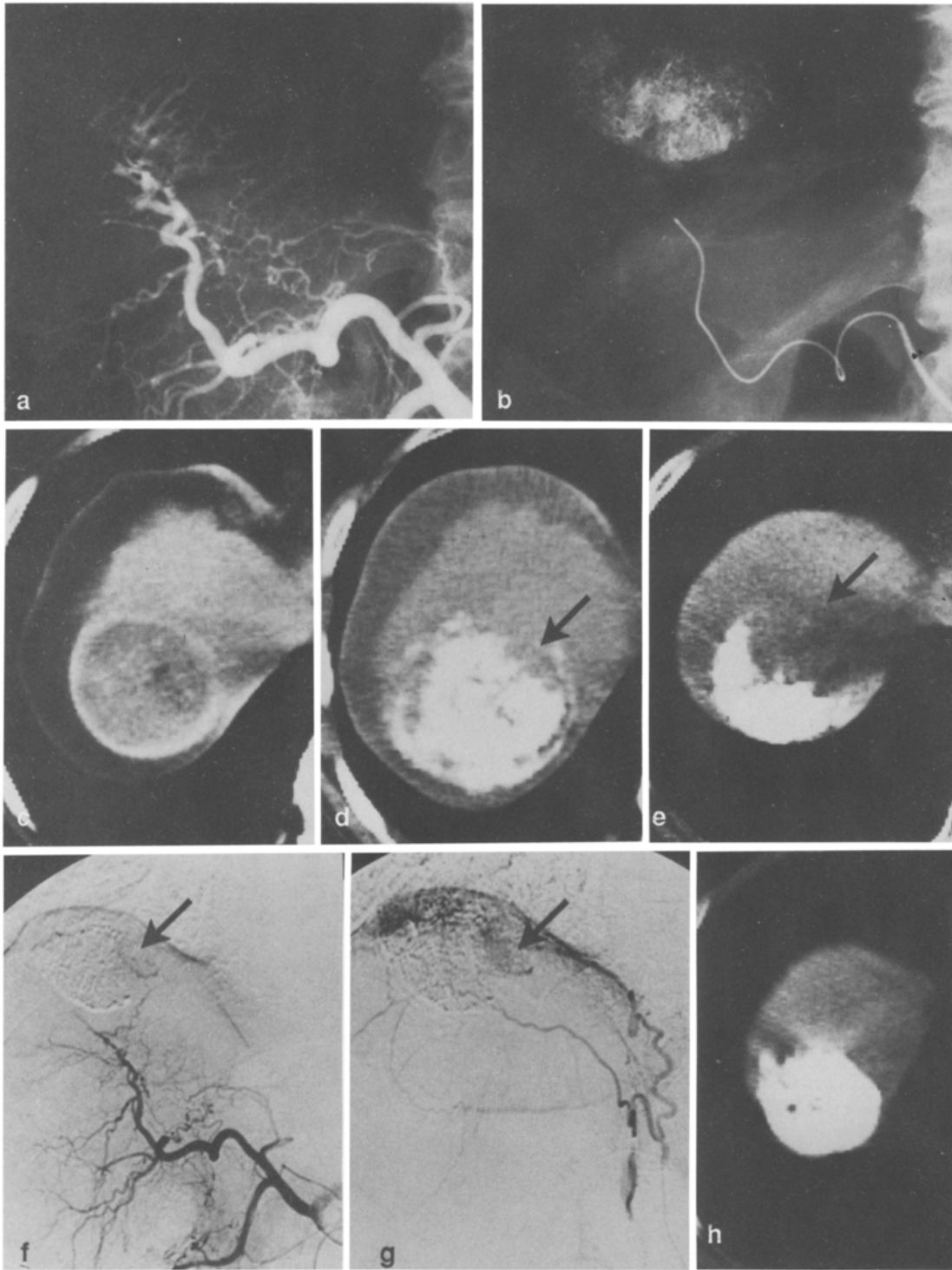
4 years, with the corresponding figures for the nodular type measuring more than 3 cm in diameter being 86.1%, 66.5%, 55.7%, and 30.3% and those for the massive type being 50.0%, 0, 0, and 0.

##### 7. Comparison of cumulative survival rates as a function of the embolized site

The cumulative survival rate of Sub-sub was the highest, being 100% at 1 year, 83.3% at 2 years, 83.3% at 3 years, and 83.3% at 4 years, with the corresponding figures for Sub being 87.2%, 69.8%, 57.1%, and 50.8% and those for Seg being 89.1%, 67.4%, 52.1%, and 28.9%.

##### 8. Relationships between Seg-Lp-CT, tumor type, and embolized site (Fig. 7)

In 23 cases of the nodular type measuring less than 3 cm in diameter, the CT patterns of Sub-sub and Sub were all type I



**Fig. 4.** A 57-year-old man who underwent subsegmental Lp-TAE using a coaxial technique for HCC in S8. A hepatic arteriogram (a) showed a hypervascular tumor in S8, and a plain X-ray film obtained after subsegmental Lp-TAE (b) showed dense Lp accumulation in the tumor. A CT scan obtained before subsegmental Lp-TAE (c) showed nodular type HCC in S8. A CT scan obtained at 4 weeks after initial

Seg-Lp-TAE (d) showed type II with a defect ( ), which became larger 10 months later (e). Recurrence of the main tumor (⇒) was recognized by hepatic (f) and right inferior phrenic (g) arteriograms, and a second Lp-TAE was performed. A CT scan obtained at 4 weeks after the second Lp-TAE (h) showed type Ib. This patient has survived for more than 5 years

(type Ia, 7 cases; type Ib, 6 cases), and the CT patterns of Seg were type I in 7 cases (type Ia, 3 cases; type Ib, 4 cases), type II in 2 cases, and type IV in 1 case (hypovascular HCC). In 41 cases of the nodular type measuring

more than 3 cm in diameter, the CT patterns of Sub-sub and Sub were type I in 9 cases (type Ia, 4 cases; type Ib, 5 cases) and type II in 9 cases, and the CT patterns of Seg were type I in 18 cases (type Ia, 4 cases; type Ib, 14 cases)

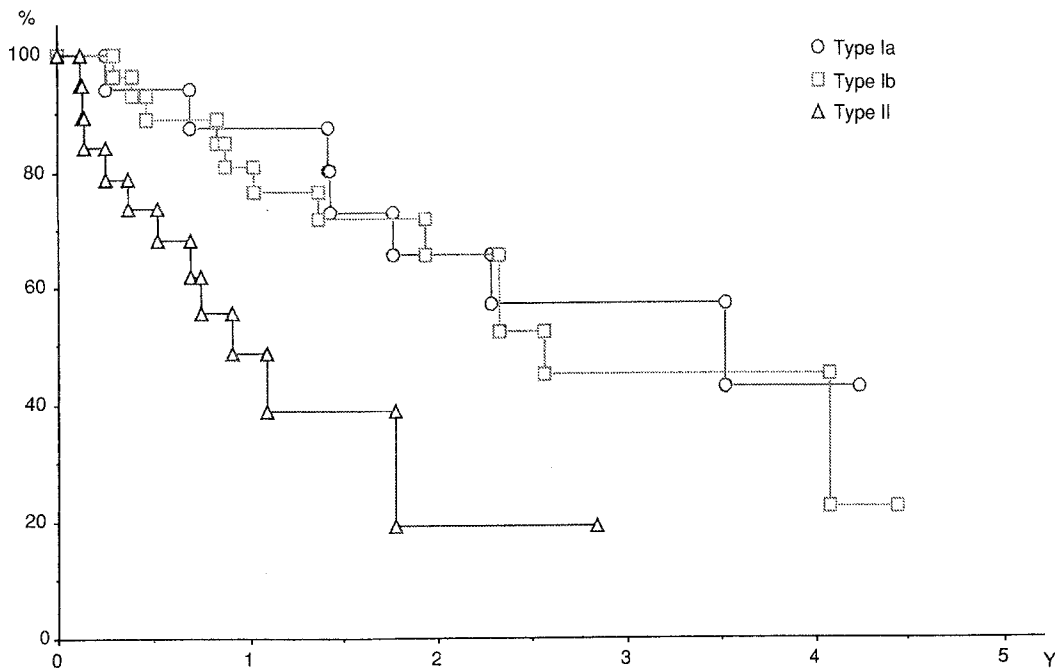


Fig. 5. Comparison of cumulative nonrecurrence rates on the basis of Seg-Lp-CT after 4 weeks

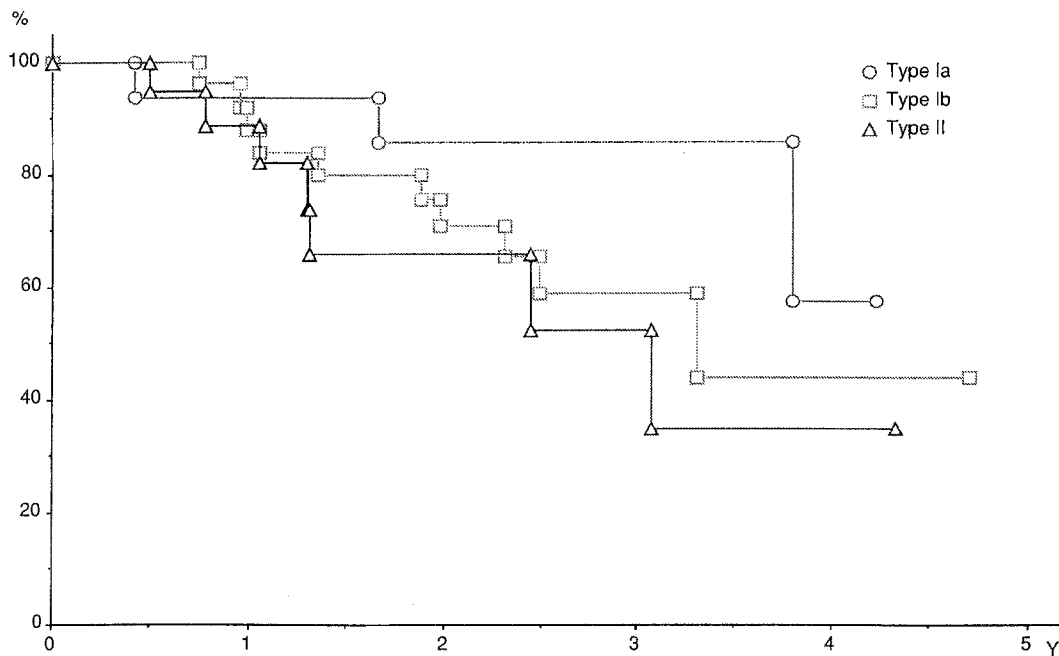


Fig. 6. Comparison of cumulative survival rates on the basis of Seg-Lp-CT after 4 weeks

and type II in 5 cases. In 9 of 18 cases (50%) of the nodular type measuring more than 3 cm in diameter undergoing Sub-sub or Sub, the type II CT pattern was recognized. In contrast, 18 cases (66.7%) of type I were achieved in Seg. In 10 of 14 cases (71%) of type II, a few feeding arteries were seen and none of them had been embolized. In three cases of the massive type, the CT patterns were all type II.

## Discussion

Recently in Japan, TAE in conjunction with an anticancer drug-Lp mixture (Lp-TAE) has been widely used in the treatment of HCC [5, 6, 12–15, 17, 20]. Although the therapeutic results of this method have shown steady improvement, recurrence of the main tumor is observed in many cases, and the therapeutic effect on capsular invasion and daughter nodules is limited. On the other hand, the

	Sub-sub	Sub	Seg
Nodular type (0-3cm)	⊙ ○	⊙⊙⊙⊙⊙ ○○○○○	⊙⊙⊙ ○○○○○ ●● ×
Nodular type (>3cm)	⊙ ○ ●	⊙⊙⊙ ○○○○○ ●●●●●●●●●●	⊙⊙⊙⊙ ○○○○○○○○○ ○○○○○○○○○ ●●●●●●●●●●
Massive type		●	●●

⊙Ia, ○Ib, ●II, ×IV

**Fig. 7.** Relationships between Seg-Lp-CT, tumor type, and embolized site

recent development of better catheters and guidewires as well as advances in angiographic techniques have made possible catheterization of the more distal branches of the intrahepatic arteries [2, 18]. For tumors limited to one segment or subsegment in patients in whom high-grade hepatic dysfunction precludes hepatic resection and in whom the adverse effects of conventional Lp-TAE on the entire liver would be undesirable, we developed Seg-Lp-TAE, which is a safe and efficacious treatment method [8, 9, 16, 18, 21]. We have previously reported on the basic concepts of this method and on the therapeutic results based on the histopathology of specimens resected after this procedure [8].

On Seg-Lp-CT performed 4 weeks after Seg-Lp-TAE, type I (in which Lp accumulated uniformly in the tumor) was found in a high proportion of cases (47 cases, 70.1%). Of those 47 cases, 18 (38.2%) showed type Ia (with Lp accumulation also being seen around the main tumor) and 29 (61.7%) showed type Ib. Also, after 2 weeks, 42 of 56 cases (75%) showed type I, which was type Ia in 38 cases (90.5%). Thus, at 2 weeks after Seg-Lp-TAE, type Ia (with Lp accumulating uniformly both in and around the tumor) was most frequently observed, although the Lp subsequently disappeared from the area around the tumor, and a tendency to shift to type Ib was seen after 4 weeks (with Lp accumulating uniformly only in the tumor). The peritumoral accumulation of Lp seen in type I is due to the retention of Lp in the hepatic arteries, portal vein, and sinusoids, with various arteriportal communications (vasa recta of the portal vein, peribiliary arterial plexus, and transsinusoidal) being surmised to play a role in the influx of Lp into the portal vein [11]. Over time, the peritumoral Lp is washed out by the portal blood flow and disappears, resulting in a change to type II.

Recurrence of the main tumor during the subsequent follow-up was found in 30 of the 67 cases in which Seg-Lp-CT after 4 weeks could be analyzed (44.8%). The recurrence rate of type I was 38% (18 of 47 cases), with no difference being seen between types Ia and Ib. The recurrence rate of type I was lower than the rates of types II and IV. Seg-Lp-CT at the time of recurrence showed types II and III in most cases, with no case of type Ia being observed. Seg-Lp-CT was useful in determining the presence/absence of recurrence. However, in six cases with type Ib on Seg-Lp-CT that showed no finding suggestive of

recurrence, angiography or dynamic CT revealed a stain in the tumor rim and recurrence was confirmed. In some cases, the evaluation of recurrence on Seg-Lp-CT when type Ib Lp accumulation is seen (with only a slight Lp defect being observed at the tumor rim) is difficult because of a partial volume effect. Accordingly, the presence/absence of recurrence must be determined by DSA, taking into account the findings of dynamic CT and MRI as well as AFP fluctuations [4].

In the study on the cumulative nonrecurrence rate, recurrence of type I cases tended to occur later than that of type II cases. In our histopathology study of cases undergoing resection after Seg-Lp-TAE, the necrosis rates of the main tumor, daughter nodules, and sites of capsule infiltration were higher in type I (particularly type Ia) cases than in type II cases [8]. These results constitute important evidence that type I is associated with a lower recurrence rate and later recurrence.

The cumulative survival rates were highest for type Ia, followed in decreasing order by types Ib and II. These results suggest that a close relationship exists between the main tumor recurrence rate and the period of recurrence with the cumulative survival rate. In type Ia the tumor necrosis rate was high; the recurrence rate, low; the recurrence period, late; and the cumulative survival rate, high, with close correlations being found among these factors. It is imperative that embolization methods be devised that are suited to individual cases so as to obtain a type Ia pattern of Lp accumulation on the CT scan.

The cumulative survival rates of the entire 98 cases undergoing Seg-Lp-TAE were 89.2%, 69.4%, 58.9%, 44.0%, and 30.2% at 1, 2, 3, 4, and 5 years, respectively. These rates were higher than the respective rates of the entire group undergoing conventional Lp-TAE [12]. In addition, they were higher than the cumulative survival rates of conventional Lp-TAE for nodular type tumors measuring  $\leq 5$  cm in diameter [12]. These results are attributed to the observations that for Seg-Lp-TAE as compared with conventional Lp-TAE, (1) the density of Lp and anticancer agent per tumor unit volume is high, (2) the antitumor effect is enhanced because Lp is infused into a more limited area, and (3) less of the Lp and anticancer agent flows out of the embolized segment into the non-cancerous portions of the liver, thereby mitigating the adverse effects of these agents on liver function.

In evaluating the therapeutic results of Seg-Lp-TAE on the basis of the cumulative survival rate, it is important to compare the results obtained with surgery and percutaneous ethanol injection therapy (PEIT). However, the advantages and disadvantages of these methods cannot be evaluated simply on the basis of the therapeutic results determined from the cumulative survival rate. This is because the cases undergoing Seg-Lp-TAE may have contraindications to surgery such as advanced liver dysfunction or high age, tumors located at sites (such as immediately below the diaphragm at S8 or adjacent to the gallbladder) in which PEIT is difficult to perform, or tumors measuring  $\geq 3$  cm in diameter, for which a marked effect of PEIT cannot be expected. In other words, Seg-Lp-TAE is performed in cases with clinical features that differ from those of cases undergoing surgery or PEIT.



The cumulative survival rates of the nodular type measuring  $\leq 3$  cm undergoing Seg-Lp-TAE were 100%, 85.4%, 73.1%, and 73.1% at 1, 2, 3, and 4 years, respectively. The corresponding rates for PEIT were 96%, 86%, 79%, and 79% in the series of Shiina et al. [19] and 100%, 100% and 80% in the series of Livraghi and Vettori [7], whereas the rates for operated cases were 91% at 1 year, 68% at 2 years, and 50% at 3 years [23]. Thus, the cumulative survival rates achieved with the three methods have been comparable. Although the invasiveness of surgery is high, it is performed only once, whereas the invasiveness of PEIT is low, but this procedure must be performed repeatedly within a short period. The advantages of Seg-Lp-TAE include its low invasiveness and the observation that a long-term effect can be achieved with the initial session. With further improvements in catheters and technique, it is thought that this method will find increasingly widespread use.

With regard to the site of embolization, the cases undergoing embolization of Sub-sub showed the highest cumulative survival rates. This finding suggests that a more distal embolization is associated with a better therapeutic effect, although another factor to take into consideration is that the cases undergoing Sub-sub embolization had smaller main tumors.

Since Seg-Lp-TAE lacks the advantage of detection of daughter nodules by Lp accumulation in the entire liver, which is achieved with conventional Lp-TAE by using a more proximal injection of Lp, recurrence cannot be avoided in the remnant liver after segmental, especially subsegmental, Lp-TAE, as in the case of subsegmentectomy. Therefore, before Seg-Lp-TAE, a precise diagnostic study of daughter nodules, especially in the non-embolized area, must be performed by US, CT, CTAP, and/or MRI. We also make every effort to detect recurrence as soon as possible after Seg-Lp-TAE using imaging diagnosis and AFP, and we repeat the therapy for recurrent tumors.

The relationship between tumor morphology and the site of embolization was investigated with Seg-Lp-CT. Among the 23 cases with nodular type tumors measuring  $\leq 3$  cm in diameter, all 13 cases undergoing Sub-sub or Sub embolization were type I, whereas 10 cases undergoing Seg embolization consisted of 7 cases of type I, 2 cases of type II, and 1 case of type IV. Of the 2 type II cases, 1 case was judged to be this type on the basis of a low-density area around the Lp thought to be due to infarction after Seg-Lp-TAE, and the 1 type IV case was thought to be a hypovascular HCC. Of the 41 cases with nodular type tumors measuring  $\geq 3$  cm in diameter, 27 showed type I, of which 18 cases (66.7%) underwent Seg embolization. The frequency of type I was higher in cases undergoing Seg than in those undergoing Sub-sub or Sub embolization. In all, 14 cases showed type II, of which 1, 8 and 5 cases underwent Sub-sub, Sub, and Seg embolization, respectively; the frequency of type II was highest in cases undergoing Sub-sub and Sub embolization. These type II cases included 7 cases in which none of the feeding arteries had been embolized, 4 cases in which parasitic feeding arteries had developed due to the presence of an extrahepatic growth or a tumor located on the segment border, 1 case in which an insufficient volume of Lp relative to the tumor diameter was infused, 1 case with a hypovascular HCC, and 1 case in which Lp was

not infused into the necrotic and organized portions. All of the three massive types were type II.

These results suggest that in the nodular type measuring  $\leq 3$  cm in diameter, embolization of more distal sites (Sub-sub, Sub) is desirable, whereas in the nodular type measuring  $\geq 3$  cm, special attention should be paid to embolize all feeding arteries, with Seg rather than Sub embolization being performed, depending on the individual circumstances.

## Conclusions

Segmental Lp-TAE is useful in the treatment of HCC limited to one segment. The most favorable therapeutic effect can be anticipated when the tumor is of the nodular type and measures less than 3 cm in diameter, the embolized site is Sub-sub, and homogeneous Lp accumulation (type I) is seen on Seg-Lp-CT. Even if the tumor is the nodular type that measures more than 3 cm in diameter and the embolized site is Sub or Seg, good results may be achieved if type I is seen on Seg-Lp-CT. Thus, it is important to choose Sub-sub, Sub, or Seg embolization according to the size and site of the tumor as well as the type and number of feeding arteries.

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