

# Outcome of localized hepatocellular carcinoma treated with segmental arterioportal chemoembolization\*

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**Summary.** When lipiodol is injected into the hepatic artery at a dose exceeding a certain level, it flows into the portal vein. On the basis of this feature, an emulsion of Adriamycin with lipiodol was injected into a segmental or subsegmental artery such that it was delivered to the portal vein of the same segment, and the artery was then embolized with Gelfoam. This segmental arterioportal chemoembolization (cement therapy) was performed in 50 patients with localized hepatocellular carcinoma. A posttreatment CT scan showed that almost 100% of the lesions were occupied by lipiodol. The cumulative survival values determined for the 50 patients were very high: 83.4% after 1 year and 62.7% after 2 years.

with Gelfoam was needed to produce complete necrosis of the main tumors.

Following these trials, we developed segmental arterioportal chemoembolization, in which an Adriamycin-in-oil emulsion is injected into the segmental or subsegmental artery, which is then embolized with Gelfoam after visualization of the portal branch of the segment. Lipiodol remained in the segment at high concentrations, and the tumor was packed and enclosed as if it had been cemented. For this reason, we named this procedure “cement therapy”. The present article reports the outcome of 50 patients who underwent this cement therapy.

## Subjects and methods

A total of 50 patients, including 36 men and 14 women aged 42–88 years (mean, 61.3 years), who had subsegmentally or segmentally localized HCC, were selected for the study. As shown in Table 1,

## Introduction

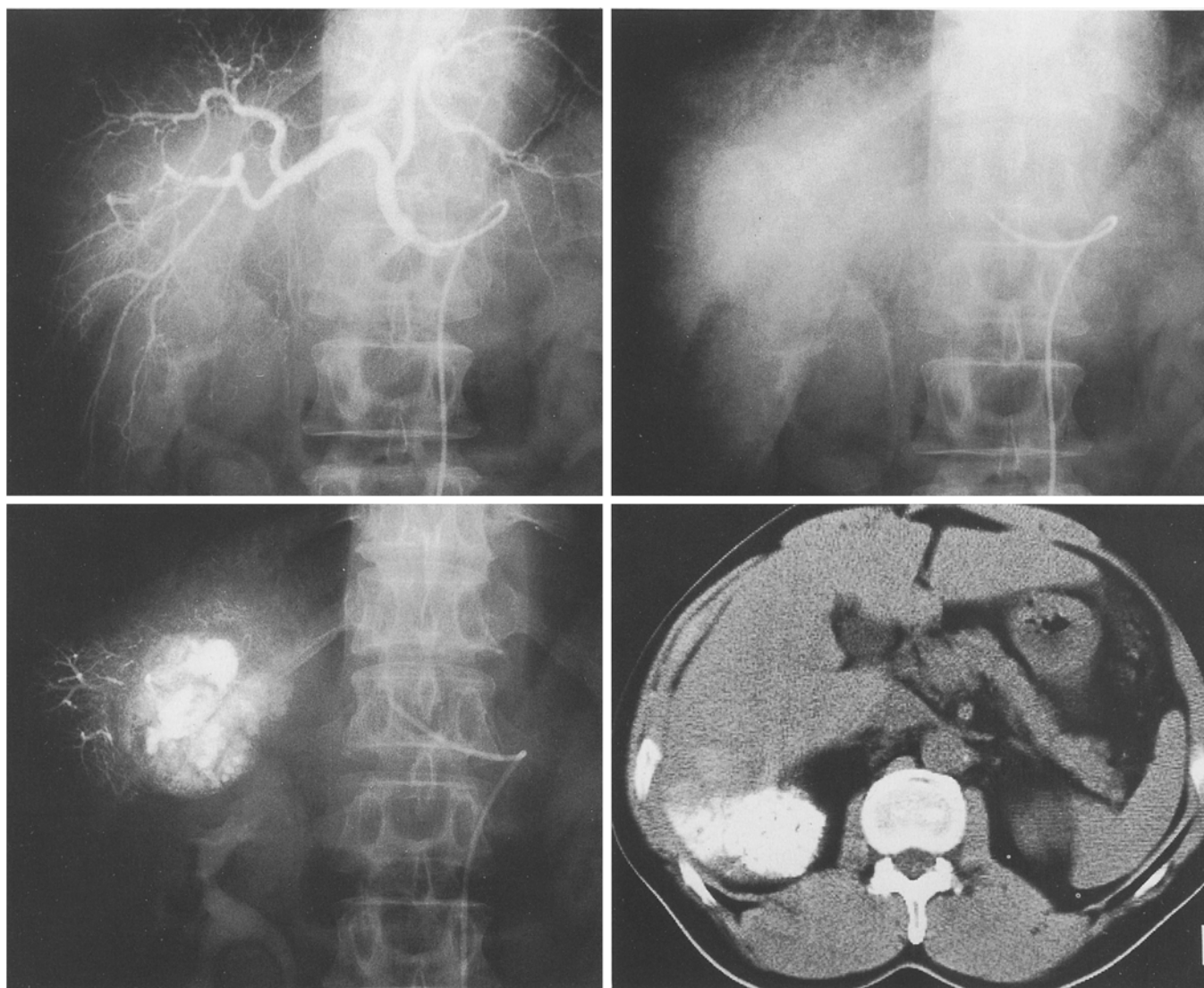
We found that the portal branches were often visualized on plain X-rays taken immediately after the injection of lipiodol at relatively high doses into the hepatic artery. We then demonstrated that this phenomenon was positively correlated with the dose of lipiodol [1]. When lipiodol was injected into the right hepatic artery of normal dogs, the portal branches in the right lobe alone were visualized. These results encouraged us to attempt the treatment of localized hepatocellular carcinoma (HCC) by injecting an emulsion of Adriamycin in lipiodol (Adriamycin-in-oil emulsion) into the segmental artery until it overflowed into the portal branch of the segment [3]. Daughter nodules, which had not responded to conventional therapy, showed a very good response to this segmental chemoembolization, but additional embolization of the segmental artery

**Table 1.** Segments treated by cement therapy

Single subsegment:								
	S <sub>2</sub>	S <sub>3</sub>	S <sub>4</sub>	S <sub>5</sub>	S <sub>6</sub>	S <sub>7</sub>	S <sub>8</sub>	Total
Number of cases	1	2	5	3	10	1	13	35
2 subsegments:								
	S <sub>2</sub> + S <sub>4</sub>			S <sub>2</sub> + S <sub>6</sub>			Total	
Number of cases	1			1			2	
Single segment:								
	S <sub>2, 3</sub>			S <sub>5, 8</sub>			Total	
Number of cases	7			4			11	
Single segment + single subsegment:								
	S <sub>2, 3</sub> + S <sub>4</sub>			S <sub>2, 3</sub> + S <sub>8</sub>			Total	
Number of cases	1			1			2	

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**Fig. 1 a–d.** A 65-year-old man with HCC treated by cement therapy. **a, b** Proper hepatic arteriogram showing a tumor with an unclear border that was detected in the right lobe by contrast staining. **c** A small catheter was inserted into the subsegmental artery ( $S_7$ ). An emulsion of Adriamycin (50 mg) with lipiodol (5 ml) was injected into the artery. Immediately thereafter, subsegmental portal veins ( $S_7$ ) become visible. **d** CT scan obtained at 10 days after the therapy. Lipiodol was retained only in the subsegment that contained the tumor

lesions were localized in single subsegments in 35 patients, in two subsegments in 2 subjects, in single segments in 11 patients, and in single segments plus single subsegments in 2 individuals.

Angiography of the common hepatic artery or the proper hepatic artery was first performed to determine the extent of the tumor by identifying the feeding artery. Then, a catheter was placed in the segmental or subsegmental artery. CNA-type 5-F catheters (Clinical Supply) or Tracker-18 infusion catheters (Target Therapeutics) were used. A water-in-oil emulsion containing Adriamycin (Adriamycin-in-oil emulsion) was prepared as follows: 40–60 mg Adriamycin was dissolved in 3–5 ml of a fluid (a mixture of 60% Urografin with distilled water at 1:5, v/v) that was equivalent to lipiodol in specific density, and the solution was then mixed with 5–10 ml lipiodol [2]. The emulsion was injected slowly via the catheter under fluoroscopic control to ensure that the portal branch was visualized in the target segment or subsegment. The segmental or subsegmental artery was then embolized with Gelfoam pellets measuring 1–2 mm in diameter (Fig. 1).

After the therapy, the patients were followed mainly by CT. CT scans were obtained at 1 and 4 weeks after the therapy and then at intervals ranging from 1 to several months. Three patients also underwent liver scintigraphy. The response was assessed on the basis of the cumulative survival of the patients.

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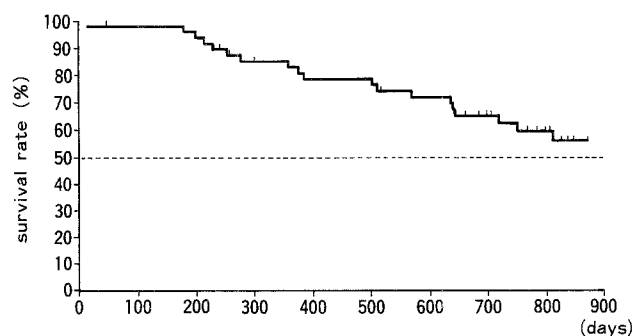
## Results

### CT and liver scintigraphy

CT revealed that lipiodol remained only in the segment into which the emulsion had been injected, and it was retained in almost 100% of the tumor volume (Fig. 1). In three patients who also underwent liver scintigraphy, radioisotope uptake clearly decreased in the target segments following the therapy.

### Therapeutic results

Figure 2 shows the survival curve (Kaplan-Meier method) generated for the 50 patients who underwent the therapy. The cumulative survival values were 83.4% after 1 year and 62.7% after 2 years.



**Fig. 2.** Cumulative survival curve (Kaplan-Meier method) generated for 50 patients with localized hepatoma after cement therapy

### Adverse reactions

The cement therapy caused more severe liver damage than did conventional chemoembolization in some patients who received it in more than one segment. In contrast, in patients with subsegmental lesions, the adverse reactions were much milder than those associated with conventional chemoembolization.

### Discussion

Transcatheter chemoembolization is an effective therapeutic modality for HCC. However, extracapsular infiltrations and small nodules do not always respond, even when lipiodol is also used, because the portal blood flow is involved in these lesions [5–7]. Moreover, arterial infusion therapy or embolization based on catheter placement in the portal vein is difficult to perform without laparotomy [4]. When oily chemoembolization [2] is carried out, the emulsion of an anticancer drug in lipiodol is delivered to the sinusoid, and it is partly refluxed to the portal vein. By this approach, it may be possible to block the portal blood supply to some extent. However, portal reflux of the emulsion would be very limited and, accordingly, this therapy has its own limitations. Moreover, when underlying hepatic dysfunction is severe, this procedure should not be applied.

In contrast, our cement therapy is very effective for the treatment of small nodules, which are likely to be fed by

the portal blood supply. The whole area subjected to the therapy, including the noncancerous normal tissues, is affected. When the lesion is localized is a subsegment, this method can be used even in the presence of extremely severe hepatic disease.

A total of 50 patients with HCC underwent the cement therapy, and their response was evaluated by the cumulative survival alone. No other criterion is appropriate for the assessment of response when embolization is the main therapy involved because both the presence and the extent of tumor regression are not always consistent with the therapeutic response. The cumulative survival values determined for the 50 patients were very high, amounting to 83% after 1 year and 63% after 2 years, although the tumors treated were relatively localized. The selection of patients for this therapy may be difficult. Cement therapy may be strongly recommended for patients in whom hepatectomy would be difficult to perform because of reduced hepatic function. We hope that cement therapy proves to be an effective substitute for hepatectomy in such cases of HCC.

### References

1. Nakamura H, Hashimoto T, Oi H, Sawada S (1988) Iodized oil in the portal vein after arterial embolization. *Radiology* 167: 415
2. Nakamura H, Hashimoto T, Oi H, Sawada S (1989) Transcatheter oily embolization of hepatocellular carcinoma. *Radiology* 170: 787
3. Nakamura H, Hashimoto T, Oi H, Sawada S, Furui S, Mizumoto S, Monden M (1990) Treatment of hepatocellular carcinoma by segmental hepatic artery injection of Adriamycin-in-oil emulsion with overflow to segmental portal veins. *Acta Radiol* 31: 347
4. Nakao N, Miura K, Takahashi H, Ohnishi M, Miura T, Okamoto E, Ishikawa Y (1986) Hepatocellular carcinoma: combined hepatic arterial and portal venous embolization. *Radiology* 161: 303
5. Ohishi H, Uchida H, Ohue S, Matsuo N, Yoshioka T, Hosogi Y, Tsuji T, Yoshida H, Fukai Y, Matsumori T (1986) Diagnostic values and therapeutic effects of transcatheter arterial embolization using lipiodol (LP-TAE) for hepatocellular carcinoma. Comparison of medical images and resected specimens. *Acta Hepatol Jpn* 27: 28
6. Takayasu K, Shima Y, Muramatsu N, Yamada T, Makuuchi M, Hasegawa H, Hirohashi S (1987) Hepatocellular carcinoma treated with intra-arterial iodized oil with and without chemotherapeutic agents. *Radiology* 162: 345
7. Yumoto Y, Jinno K, Tokuyama K, Araki Y, Ishimitsu T, Maeda H, Konno T, Iwamoto S, Ohnishi K, Okuda K (1985) Hepatocellular carcinoma detected by iodized oil. *Radiology* 154: 19