

Comparative study of epirubicin-iodized oil suspension and emulsion in rabbit VX2 liver tumor by transcatheter arterial chemoembolization

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Introduction

Transcatheter arterial chemoembolization (TACE) plays a major role in the treatment of advanced hepatocellular carcinoma. Until now, various formulations of anticancer agents-iodized oil such as emulsion and suspension have been evaluated for TACE.

Suspensions have been reported to demonstrate sustained release and antitumor effect. Some reports indicate that suspension is more effective than emulsion, but no reports have compared the antitumor effects of epirubicin-iodized oil suspension and emulsion for TACE.

Purpose

To evaluate antitumor effects of TACE with the use of epirubicin-iodized oil suspension and emulsion in a rabbit model.

Material and Methods

- ◆ Ten rabbits with VX2 liver tumor were divided into two groups.
- ◆ TACE was performed with **epirubicin suspension or emulsion.**

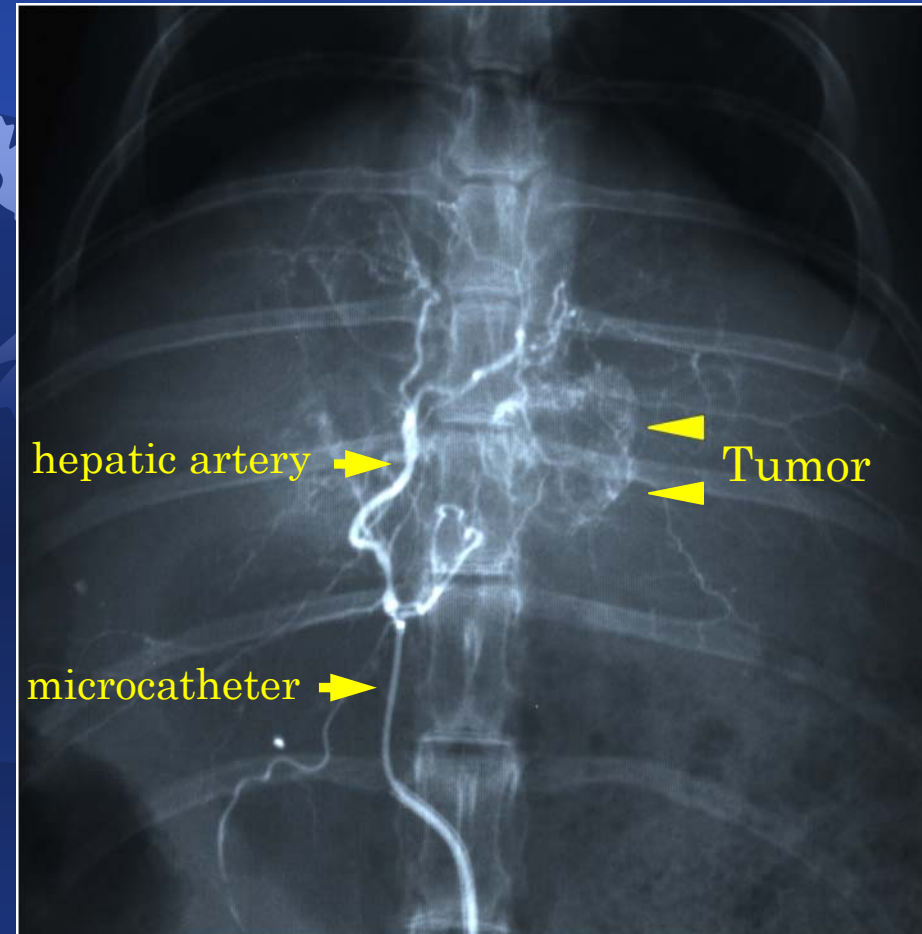
suspension group (n=5)

0.5 mg/kg epirubicin
+ 0.1 ml/kg iodized oil

emulsion group (n=5)

0.5 mg/kg epirubicin
+ 0.1 ml/kg NaCl solution
+ 0.1 ml/kg iodized oil

Middle hepatic arteriography



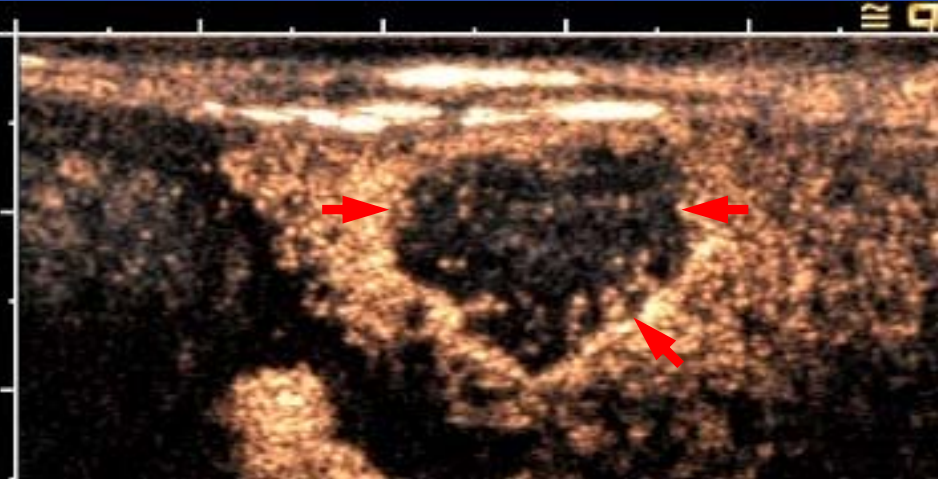
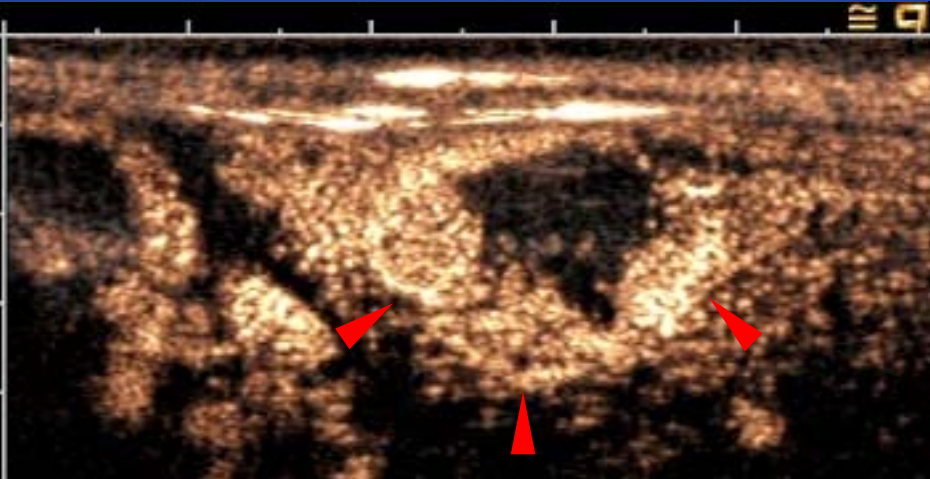
Material and Methods

- ◆ Seven days after TACE, all rabbits were sacrificed, and **the growth ratio and viable proportion of tumors** was calculated on the basis of Sonazoid-enhanced ultrasonography and histopathological examination.
- ◆ Sustained release was evaluated by changes in **plasma epirubicin concentration** over time.
- ◆ Differences between the two groups were statistically assessed.

Sonazoid-enhanced Ultrasonography

A) Arterial phase

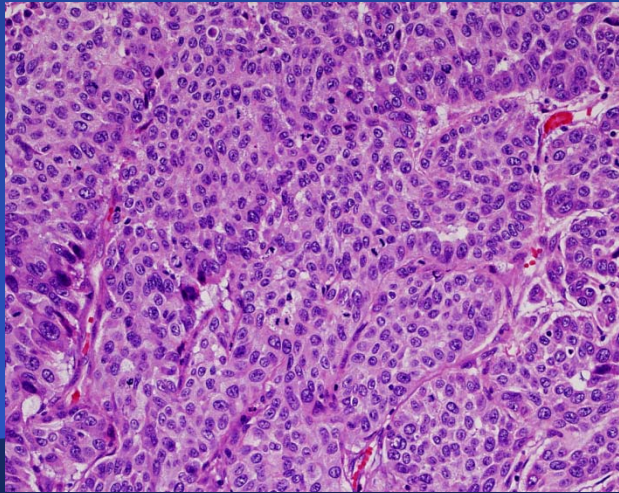
B) Kupffer phase



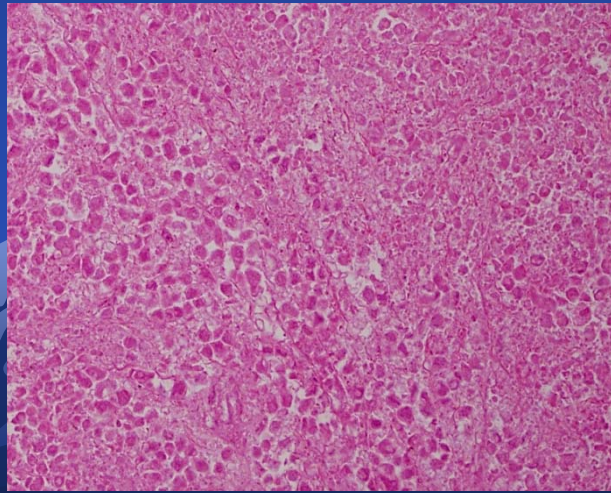
- A) Immediately after administration of Sonazoid, the tumor shows a strong contrast effect depending on vascular distribution, especially in the marginal area.
- B) Only the tumor lacks contrast effect 10 minutes after administration of Sonazoid, and the edge can be clearly visualized.

Histopathological Examination

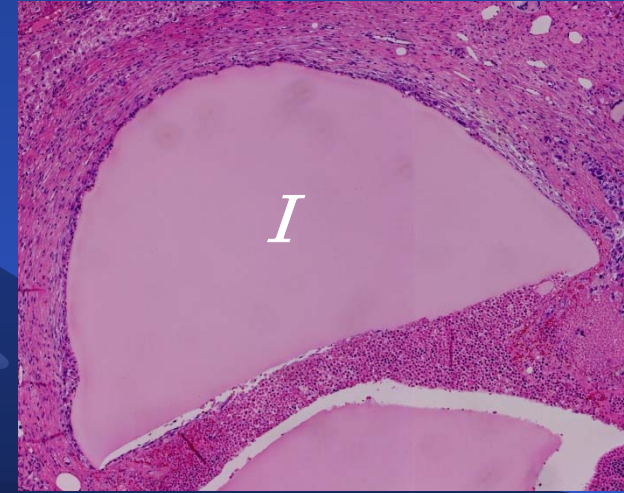
A) viable portion



B) necrotic portion



C) destructive vascular structure

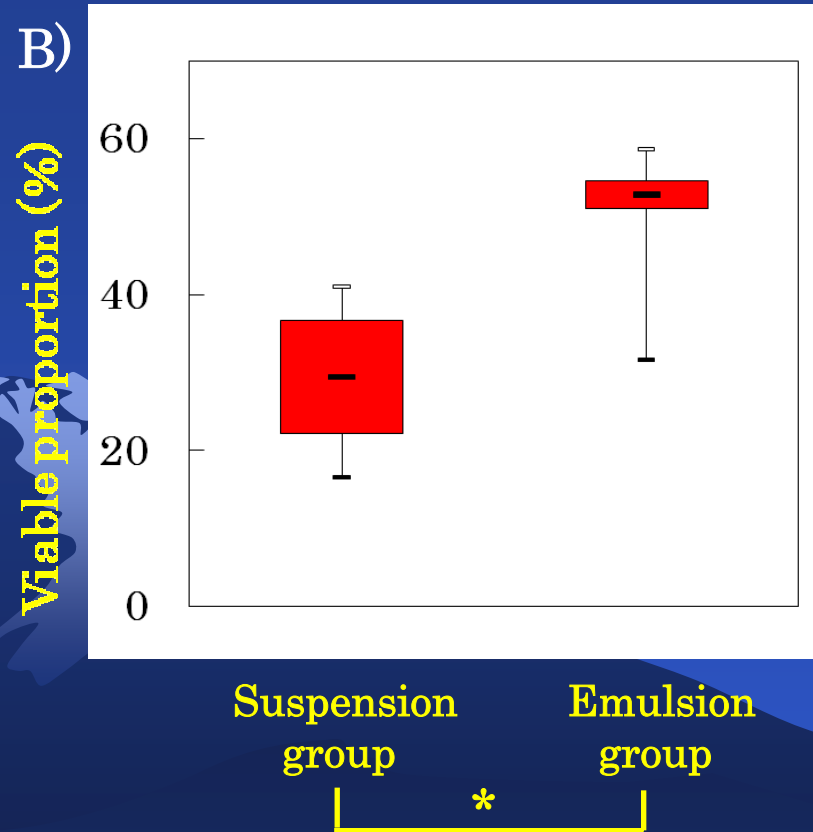
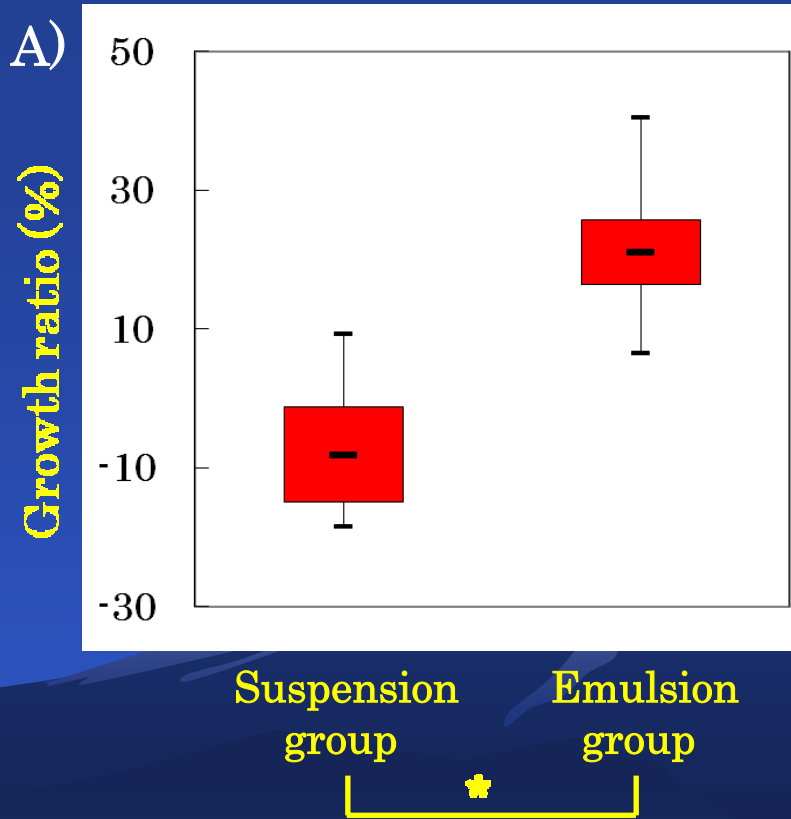


A–C: hematoxylin-eosin stain; original magnification, 20×
I = iodized oil

In the viable portion (A), cellular colonies with adequately stained nuclei and cytoplasm are observed, but they are not observed in the necrotic portion (B).

A deposit of iodized oil remains in the destructive vascular structure (C).

Result (Growth Ratio and Viable Proportion)



*:P < 0.05 (Mann-Whitney U test)

- A) Growth ratios of the tumors in the suspension group ranged from -18.4% to 9.4% ($-7.3\% \pm 11.3\%$ [mean \pm SD]). In the emulsion group, tumor volumes increased from 6.6% to 40.4% ($21.4\% \pm 12.6\%$).
- B) Viable proportion of tumors ranged from 16.6% to 41.1% ($28.0\% \pm 10.4\%$) in the suspension group, and from 31.6% to 58.7% ($49.6\% \pm 10.5\%$) in the emulsion group.

Result

Plasma Epirubicin Concentration (ng/mL)

Time (h)	Suspension (n=5, mean \pm SD)	Emulsion(n=5, mean \pm SD)	P*
0	205.73 \pm 120.14	173.20 \pm 110.58	0.69
0.5	3.53 \pm 1.25	2.18 \pm 1.90	0.26
1	3.55 \pm 1.05	1.26 \pm 1.22	0.02
3	2.33 \pm 0.85	1.38 \pm 1.33	0.26
6	1.06 \pm 1.93	1.32 \pm 1.42	0.81
24	0.98 \pm 1.28	0.62 \pm 0.85	0.63

* unpaired t-test

Discussion I

The growth ratios in the suspension group were significantly smaller than those in the emulsion group, and the viable proportion of tumor in the suspension group was also significantly smaller than that in the emulsion group.

Therefore, **suspension appears to demonstrate a greater antitumor effect than emulsion.**

Discussion II

The epirubicin concentration in the suspension group was significantly higher than that of the emulsion group at 1 hour after administration. The results indicate that epirubicin stayed in the tumor for a longer time in the suspension group and was distributed more slowly to plasma. Consequently, **the suspension may provide greater sustained release than the emulsion.**

Concluisons

The use of epirubicin-iodized oil suspension is superior to that of emulsion in terms of antitumor effects for rabbit VX2 liver tumor.

Thank you very much for your attention

