

Hepatocellular Carcinoma; Treatment with a Radioiodinated Fatty Acid Ester

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It has been shown that iodinated fatty acid esters such as Ethiodol () or Lipiodol(**) are selectively retained in hypervascular hepatic tumors following intrahepatic arterial administration. Such agents have been utilized in the detection and treatment of hepatocellular carcinoma (HCC) along with anticancer drug emulsions. Radioiodination of Lipiodol (I-131-Lipiodol) was achieved by using a simple exchange method and the agent was used in the treatment of HCC following intrahepatic arterial injection via superselective catheterization of tumor feeding vessels. Forty patients with HCC (massive 18; multinodular 12; infiltrative 10) were treated in an attempt to deliver a high dose of internal radiation; a cumulative tumor dose of 12,000 rad (120 Gy) or higher was aimed in single or multiple procedures. Following therapy, the patients were divided into 2 groups, responsive or nonresponsive. Patients classified as massive type responded to this treatment best (72.3%) followed by multinodular type (33.3%) and infiltrative type (10.0%). According to the size of tumor there was an 80.0% response for tumors of less than 5cm in diameter, 60.0% between 5 to 8cm and 9.0% larger than 10cm in diameter. The clinical results of this treatment modality appear to be quite promising in the management of HCC, especially in the less than 8cm sized massive type of HCC. Also this method was able to not only provide long term local control but also a good quality of life without complications.*

Key Words: Hepatocellular carcinoma, I-131-Lipiodol, interventional radiology

Frequent association of hepatitis B virus (HBV) and hepatocellular carcinoma (HCC) is present among people in the Far East as well as in other endemic regions.

HCC is one of the most common malignant neoplasms in the Far East and its prognosis with conventional treatment is extremely poor with an average survival of six months (Okuda 1986). There has been no effective treatment except for the early stage of the disease. Even though the tumor may be small in size surgical resection, however, is often not indicated

because of an associated cirrhosis. Therefore, development of a new therapeutic modality for HCC is urged under the present circumstances. Japanese scientists have found selective localization of Lipiodol within hypervascular HCC following intrahepatic arterial injection (Iwai *et al.* 1984; Nakakuma *et al.* 1979; Ohishi *et al.* 1985).

As a result, Lipiodol chemotherapeutic emulsions were successfully used for the treatment of HCC (Kono *et al.* 1983; Ohnishi *et al.* 1984) as well as for the detection of hepatoma and daughter nodules (Nakakuma *et al.* 1985; Ohishi *et al.* 1985; Yumoto *et al.* 1985).

The purpose of this study is to introduce a new treatment modality using a radioiodinated fatty acid ester (I-131-Lipiodol) for the treatment of HCC and to assess the therapeutic efficacy.

Radioiodination of Lipiodol can be achieved by a simple exchange method. We have tried therapeutically feasible studies using this material in an attempt to deliver a high dose of internal radiation to HCC (Park *et al.* 1986; Yoo *et al.* 1986). Forty patients with HCC were treated with I-131-Lipiodol via an in-

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terhepatic arterial injection.

Preliminary clinical results of I-131-Lipiodol in patients with HCC are presented in this report.

MATERIALS AND METHODS

Characteristics and selection of patients

A total of forty patients with inoperable HCC were selected for therapeutic trial with I-131-Lipiodol from Feb. 1986 to May 1987 and followed up for three to eighteen months after treatment. The patients ranged in age from 35 to 72 years, and the mean age was 51 years. There were 34 males and 6 females.

For the purpose of this study, HCC was divided into three groups; massive, multinodular and infiltrative in accordance with CT and angiographic findings. Massive type refers to a solitary, well-encapsulated tumor ranging in size from 2.0cm to 12cm. There were 18 cases in this group. The multinodular type presents with multiple nodules which were also hypervascular. Among the 12 multinodular types, there were 5 cases of recurrent tumor after segmentectomy of HCC. Ten cases were included in the infiltrative type group. Thirty-two (80%) of the patients also exhibited liver cirrhosis.

The criteria for patient selection for the therapeutic protocol were the following:

- 1) Hypervascular HCC on arteriogram.
- 2) Superselective injection possible.
- 3) Three to ten cm sized tumor requiring less than a total of 60 mCi of I-131.
- 4) No clinical or radiologic evidence of metastatic disease.
- 5) Underlying cirrhosis is not contraindicated.

Patients with the following conditions were excluded from the study.

- 1) Allergic to iodine
- 2) Severe chronic lung disease.
- 3) Portal vein involvement by the tumor.
- 4) Significant arteriovenous shunting of the tumor.

Initial and follow-up studies

Baseline studies included laboratory tests, such as hepatitis surface antigen (HBs Ag), alpha feto protein (AFP), liver function tests (LFTs), radionuclide scintiscan (Tc 99m-sulfur colloid, Ga-67 scan) ultrasonography, hepatic computed axial tomography (CT), arteriography, and aspiration cytology. The final diagnosis of HCC was made by cytology (NAB, 24 cases), elevated AFP with abnormal diagnostic images (11 cases), and open biopsy (5 cases). Follow-up studies

were performed with serial measurements of AFP, and periodic study with CT, ultrasonography, Ga-67 scintiscan and angiography for assessment of tumor response and the possibility of surgical resection.

Assessment of tumor response was classified into two groups, responsive or nonresponsive.

Responsive was defined as decreased tumor volume as measured by serial ultrasonography and/or CT scans, decreased tumor uptake on Ga-67 scans, and decreased AFP levels, for more than 3 months following the treatment. The non-responsive group demonstrated continuous tumor growth following the imaging studies and elevation of AFP levels during the follow-up period.

Radioiodination process

Lipiodol has 30% iodine (stable I-127) by weight. A small fraction of stable iodine is replaced with radioactive I-131 by a simple exchange method described below.

High specific activity I-131 is boiled in 0.1M NaOH to dryness in the presence of 0.5mg of potassium iodide. The residue is refluxed in 25ml of acetone for 20 minutes, and then 1-2ml of Lipiodol is added. The solution is again refluxed for another thirty minutes.

The acetone is removed using a rotating evaporator in a 70°C water bath.

The residue is cooled, placed in a sterile vial and autoclaved by boiling in butanol. The labeling efficiency has been found to be greater than 99%, and the agent has been stable in vivo.

Method of administration

An arterial catheter was inserted into the femoral artery and was advanced to the branches of the hepatic artery supplying the tumor.

Three to fifteen ml of I-131-Lipiodol depending on the tumor size were injected into the hepatic arterial branches at a rate of 10-20ml/hr either manually or via an automatic injection syringe. Superselection of the hepatic arterial branch requires a highly skilled technique.

Dose range

I-131 has a half life of 8.05 days, a gamma radiation of 364 KeV, and an average beta energy of approximately 190 KeV. A gamma camera was used for biodistribution imaging study which is suitable for therapy using the Quimby method, a total cumulative tumor dose of 12,000 cGy (120 Gy) was aimed initially. An escalating dose of up to 20,000 cGy (200 Gy) was

Table 1. Relationship among tumor size, I-131-Lipiodol activity and Lipiodol volume. (Approximately 12,000 rad protracted radiation was aimed at the tumor)

Tumor size (cm)	Tumor Vol. (gm)	Rad/mCi	I-131 in tumor (mCi)	Volume of Lipiodol (cc)
1	0.52	167,682	0.07	1.5
2	4.18	21,380	0.56	3.0
3	14.13	6,479	1.85	4.5
4	33.49	2,798	4.28	6.0
5	65.41	1,466	8.18	7.5
6	113.04	867	13.84	9.0
7	179.50	558	21.50	10.5
8	267.94	382	31.41	12.0
9	381.51	274	43.79	13.5
10	523.33	204	58.82	15.0

tried laterly. The dose of I-131 and the volume of Lipiodol were dependent upon the size of the tumor. A calculated dose ranging from 5-60 mCi of I-131 was delivered depending on the tumor volume as computed by 9mm sliced of CT scan (Table 1).

Biodistribution and quantification studies

Prior to the therapeutic trial of I-131-Lipiodol, the distribution and kinetics of the radiolabeled I-131-Lipiodol was studied in twelve patients diagnosed with HCC.

Transmission images of the lung and liver regions were acquired on the scintillation camera interfaced to compute in order to obtain the transmission factors. This was performed prior to the administration of the I-131-Lipiodol using approximately 1 mCi of I-131 in solution in a flood field phantom.

Then calibration factor (system sensitivity) is obtained using an accurate of I-131.

A collimator designed for I-131 was used and a 20% window was centered on the 364 KeV photopeak for these studies. The radioactivity in the syringe and catheter was assayed in a dose calibrator both before and after administration so that the administered amount was accurately known. Following injection, anterior images of the lungs, liver, thyroid and spleen regions were acquired and stored on a computer. For the following 2-3 days, anterior and posterior scintigraphic views of the liver, lung, thyroid and pelvic regions were obtained along with an I-131 standard. Then, calculations of the dose to the tumor, the dose to the normal liver, the dose to the lungs and whole body were performed. Blood samples were taken and the urine was collected.

Tumor to Nontumor Ratio

Of seven patients, single photon emission computed tomography (SPECT) was obtained, and the tumor-to-normal liver or lung ratio was evaluated by comparing pixel counts over these regions.

Tumor volume studies

Tumor size was assessed from both ultrasonography and computed tomography images, and subsequent measurements of changes in size after treatment were made based on both modalities.

For practical comparison of tumor size on US images, the diameter (when round) or its equivalent ($\sqrt{a \times b}$) in the two-dimensional image was used, where a is the longest axis and b is the shortest axis perpendicular to it.

The tumor volume was calculated by either $4/3\pi r^3$ or $4/3\pi(\sqrt{a/2 \times b/2})^3$.

Tumor volumes was also measured with CT scans by means of a summation of each sectional volume of tumor obtained by computer based Joy-stick measurements.

Tumor volumes were compared at the time of pre embolization and subsequent post-embolization periods.

Effective half life

Tumor effective half life (TE) was measured using sequential images stored on the computer. A region of interest over the desired area from the sequential images was selected, and the counts were plotted against the number of days imaged. The same could be done for normal organs such as the liver and lungs

to estimate radiation dose.

RESULTS

Clinical

Eighteen of 40 cases (45%) responded to this treatment modality. The patient's age, sex and Child class did not influence the response rate, however, the type and size of the tumor were important factors in the determination of the response rate to the therapy (Table 2).

The response rate according to the size of tumor was 72.3% in massive, 33.3% in multinodular, and 10% in the infiltrative types, respectively.

The response rate according to the size of the tumor was most prominent in those case of less than 5cm (80.0%), followed by 5-8.0cm (60%) and 8-10cm (33.3%).

Only one of 12 HCCs large than 10cm in diameter responded to the therapy (9.0%) (Table 3).

The 22 cases in the non-responsive group consisted of multinodular (8) and infiltrative (9) tumor types, and 10 cases had tumors larger than 10cm in diameter.

Among the responders, 9 patients are still alive more than 1 year.

Table 2. Comparison of age, sex, Child class, type and size of the tumor between the response and Non-response groups

	Response group (N=18)	Non-response group (N=22)
Age		
Mean±SD	51.8±9.4	50.2±7.5
Range	39-72	32-67
Sex (M/F)	14/4	20/2
Child Class		
A	14	14
B	4	6
C	0	2
Cirrhosis (+)	13	17
Type of Tumor		
Massive	13	5
Multinodular	4	8
Infiltrative	1	9
Size of Tumor (cm)		
- 4	8	2
5 - 7	6	4
8 - 9	3	6
10 -	1	10

Tumor to non-tumor ratio

The tumor to non-tumor ratio was measured in patients with the massive type of tumor using SPECT. When the I-131-Lipiodol was injected into the superselected tumor feeding vessels, the tumor to non-tumor ratio was approximately 10-15:1 and those with injection at the level of proper hepatic artery was approximately 5-10:1.

There was virtually no activity shown in the thyroid, bowels and bone marrow. However, less than 5% radioactivity appeared in the lung parenchyme, depending on the arterio venous shunt of the tumor.

Adverse reactions;

The patients were observed for possible side effects, but neither symptoms nor changes in the vital signs developed after infusion of radioactive iodized oil. Patients complained of slight pain in the area of the liver during infusion, and temporary abdominal pain and transient mild fever developed within a few

Table 3. Response Rate according to Type and Size Tumor

	Total No. of Cases (N=40)	No. of Res- ponse Cases (N=18)	Response Rate (%)
Type of Tumor			
Massive	18	13	72.3
Multinodular	12	4	33.3
Infiltrative	10	1	10.0
Size of Tumor (cm)			
- 4	10	8	80.0
5 - 7	10	6	60.0
8 - 9	9	3	33.3
10 -	11	1	9.0
Total	40	18	45.0

Table 4. Adverse Reaction to Treatment with I-131-Lipiodol (40 cases)

Adverse reaction	No. of cases	Percent
Moderate fever	28	70.0
Abdominal pain	15	37.5
Anorexia	5	20.0
Dyspnea	2	5.0
Pleural effusion	1	2.5
Ascites	0	0

days after infusion. Liver function tests revealed a transitory elevation of the serum SGOT and SGPT levels for a few days which returned to normal levels.

There were no abnormal changes in the bilirubin, alkaline phosphatase or BUN levels (Table 4).

ILLUSTRATED CASES

Case 1.

A 65 year old man who had a history of liver cir-

rhosis was admitted because of bleeding from esophageal varices.

CT demonstrated an 8cm well defined mass with a necrotic area in the Rt. posterior segment of the upper lobe which was confirmed as HCC by aspiration cytology (Fig. 1a). This lesion was hypervascular on celiac angiography.

Ten ml of I-131-Lipiodol containing 30 mCi of radioactivity was infused slowly into the superselected Rt. hepatic artery. I-131-Lipiodol deposition in the tumor was well visualized on subsequent angiography

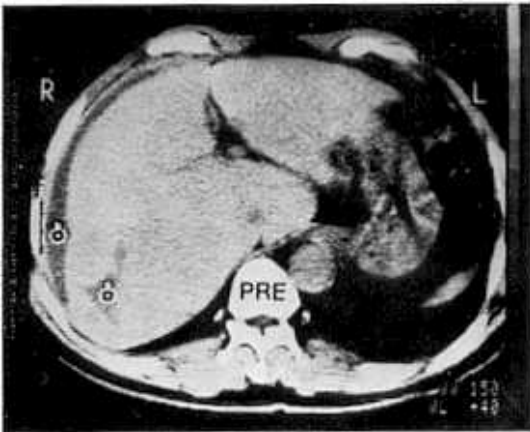


Fig. 1a. An 8cm sized well defined low density mass with necrotic area is seen in the Rt. posterior segment of the upper lobe.

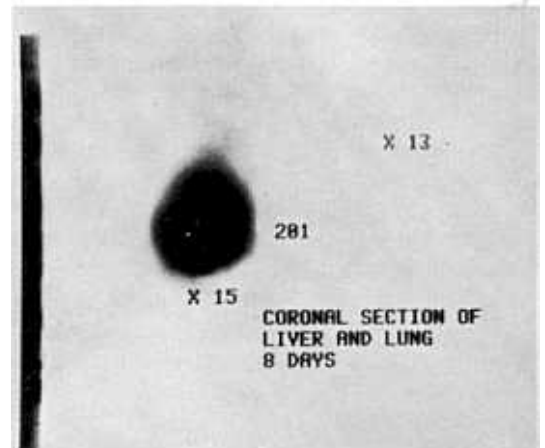


Fig. 1c. Single photon emission computed tomography (SPECT) discloses high tumor to normal liver and lung ratios on the same pixels counts.



Fig. 1b. I-131-Lipiodol angiography reveals Lipiodol deposition only in the hypervascular tumor area.

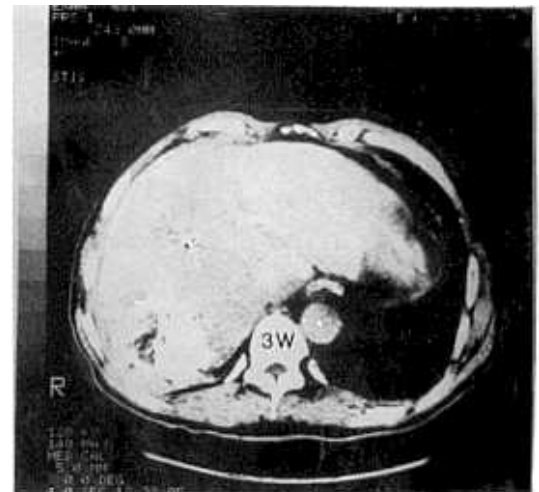


Fig. 1d. Follow-up CT scan discloses Lipiodol densities only in the tumor area.

(Fig. 1b). No daughter nodules were demonstrated.

Single photon emission CT scan was performed six days after infusion and the tumor to non tumor ratio of the liver and to lung ratio were calculated by comparing the pixel counts over these lesions. The tumor to lung ratio was about 15:1 (Fig. 1c).

An intratumoral high accumulation density of Lipiodol was confirmed by CT scan (Fig. 1d).

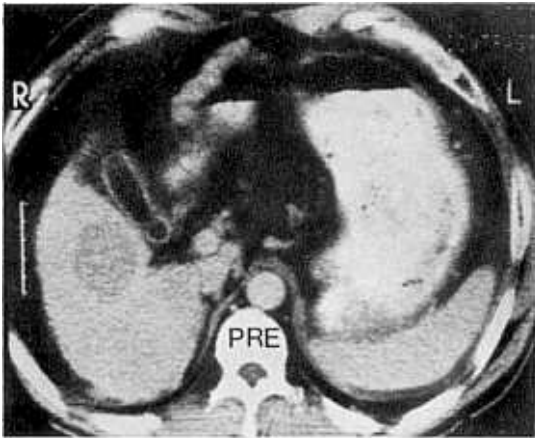


Fig. 2a. CT scan reveals a well defined low density mass in the right lower lobe and ascites.

Case 2.

A 54 year old man was admitted with advanced liver cirrhosis. On CT examination, a 5cm sized low density mass was identified in the Rt. lobe of the liver which was incidentally confirmed as HCC by aspiration cytology (Fig. 2a).

Seven ml of radiolabeled Lipiodol containing 20 mCi of activity was infused through the tumoral feeding vessel under superselection. A follow-up gamma scan revealed radioactivity confined in the tumor even 32 days after infusion (Fig. 2b).

A one month follow-up CT examination showed

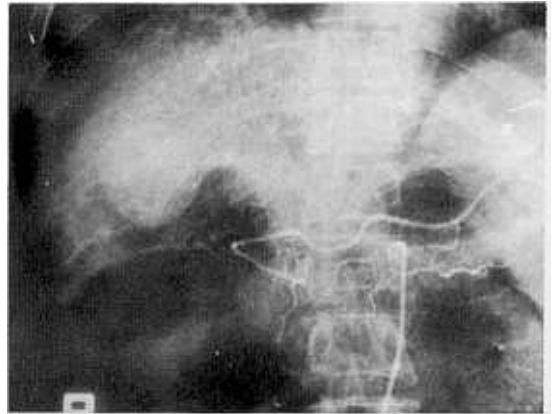


Fig. 2c. Pre treatment angiographic shows a hypervascular mass consistent with the massive type of HCC.

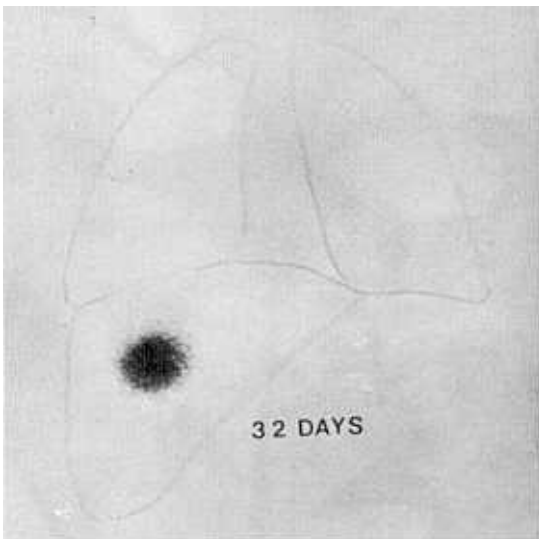


Fig. 2b. I-131-Lipiodol radioactivity is still seen in the tumor area even after 32 days in the follow-up period.

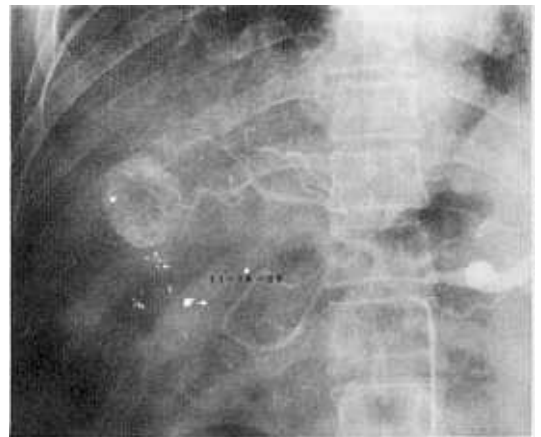


Fig. 2d. 9 month follow-up angiography depicts a contracted mass with central radiolucency suggestive of tumor necrosis.

Lipiodol density only in the tumor, and a 9 month follow-up angiography disclosed a contracted tumor with less vascularization and central necrosis as compared to that of the preembolization angiography (Figs. 2c and 2d).

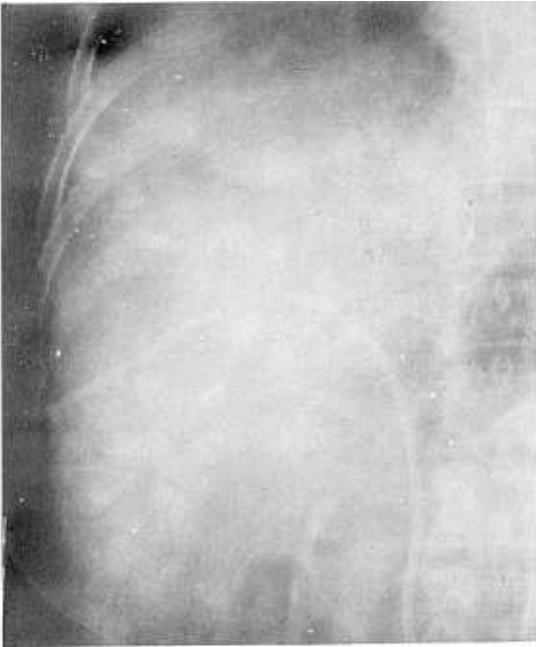


Fig. 3a. Multinodular recurrent hepatomas are seen on plain abdomen x-ray after I-131-Lipiodol injection.

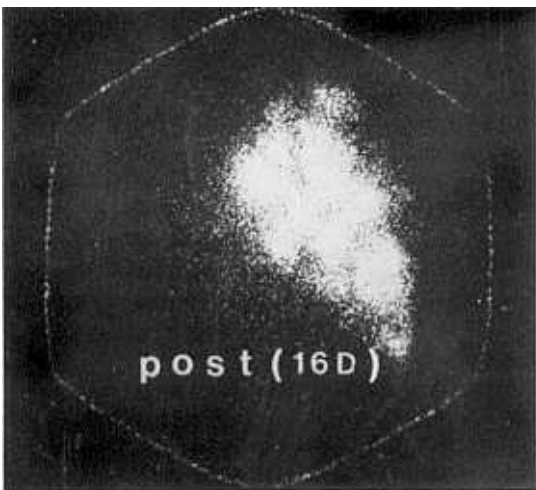


Fig. 3b. Multifocal hot uptakes are seen on gamma scan consistent with I-131-Lipiodol uptake in each tumor nodule.

Case 3

A 64 old female who had had a Lt. lobectomy in July, 1985 for hepatoma was found to have a markedly elevated AFP (12,800 ng/ml) and recurrent multifocal nodular masses in the Rt. lobe of the liver on CT examination.

Ten ml of I-131-Lipiodol containing 30 mCi of radioactivity was injected into the proper hepatic artery, and plain abdominal x-ray after injection revealed multinodular hepatomas (Fig. 3a).

Serial hepatic gamma images were obtained at four day intervals.

Even 16 days after injection, radioactivity in the multifocal tumor nodules was still seen (Fig. 3b).

The AFP level decreased to 3,200 ng/ml at the time



Fig. 4a. Angiography reveals an 8cm sized hypervascular mass in the right upper lobe of the liver.



Fig. 4b. Angiography at the time of 3 month follow-up after I-131-Lipiodol treatment reveals a markedly contracted tumor mass with devascularization.

of the 4 week follow-up. The patient survived 6 months after the treatment with clinical improvement.

Case 4.

A 52 year old man was admitted with right upper abdominal pain. CT examination revealed an 8cm sized low density mass in the right upper lobe, and a Ga-67 scans showed hot radio uptakes within the tumor bearing area. Aspiration cytology confirmed the diagnosis of hepatocellular carcinoma and angiography revealed a hypervascular mass (Fig. 4a).

Twelve ml of I-131-Lipiodol containing 40 mCi of activity was infused into the right anterior superior hepatic artery.

The three month follow-up ultrasonography and angiography revealed a tumor markedly decreased

in size and vascularity as well (Fig. 4b).

A follow-up Ga-67 scan at the same time showed a cold defect which was previously hot (Fig. 4c and 4d).

No definite tumor cells were identified on aspiration biopsy after a 4 month follow-up period.

DISCUSSION

Substantial efforts have been made during the past few years to target cancer drugs to hepatocellular carcinoma including polyclonal antibody conjugation with radioactive iodine, arterial infusion of anticancer agent such as mitomycin C or Styrene Maleic Acid Neocarzino Statin (SMANCS) with lipid lymphographic agent, and embolization with sponge gel or Ivalon particles (Ariel. 1965; Ettinger *et al.* 1982; Konno *et al.* 1983; Leichner *et al.* 1983). However, the effectiveness has been shown to be still inadequate for the treatment of HCC mainly because of the rapid development of collateral vessels within 2 to 3 weeks, and the recurrent nature of the tumors.

It is a well known fact that Lipiodol is selectively deposited in the hepatocellular carcinoma, remains for a long period of time and is used for the detection of small daughter nodules which can not be seen in conventional angiography and computed tomography examinations.

Recently, Order *et al* (1985) reported on a preliminary study of isotopic immunoglobulin therapy for primary liver cancer using anti-CEA and antiferritin antibodies labeled with I-131.

In this report 50 and 100 mCi of I-131-labelled IgG was administered to patients with hepatocellular carcinoma.

However, the systemic administration of radioactive isotopes has yielded rather disappointing results.

Iwai *et al* (1984) reported that by using low KVP X-ray examination of resected rabbit livers, Lipiodol was found to be distributed throughout the entire liver arterial lumina, was retained there for about 24 hour, but disappeared from the normal liver arterial lumina gradually. However, an important finding was the retention of Lipiodol in the tumor for long period of time.

Regarding those facts, we thought that if it were possible to replace the stable iodine with radioactive iodine of I-131, then the internal radiation might be effective on the hepatocellular carcinoma, and at the same time, the micro embolization effectiveness of the Lipiodol itself would be expected.

The I-127 content of Lipiodol was replaced with

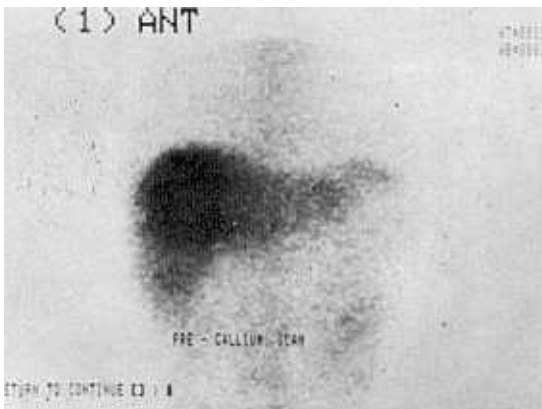


Fig. 4c. Ga-67 scan before treatment shows hot uptake in the tumor area.

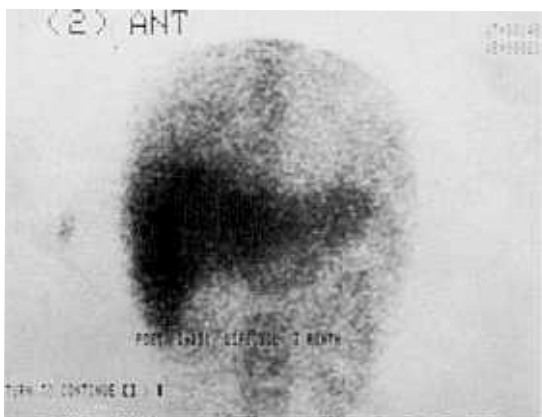


Fig. 4d. Ga-67 scan after treatment shows decreased uptake in the tumor as compared to prior therapy.

I-131 by an exchange method and confirmed the labeling efficiency of 99% by paper chromatography. Use of this material enabled delivery of a high dose of internal radiation to the tumor by intraarterial hepatic injection. A high dose of internal radiation (120-200 GY) was aimed at the tumor to treat the HCCs after tumor dose calculations using the Quimby method were determined. For effective therapy with radionuclides, there must be a high tumor to non tumor ratio.

The radiation dose should be concentrated in the tumor region, and nontarget normal tissue should receive the lowest possible dose.

In addition to selective localization of radionuclides in the tumor, the effective time over which the radiation is delivered should be sufficiently long. In our studies, infusion into the superselected tumor feeding vessel was confirmed by a radioactivity of 10 to 15 times over the non tumor tissue of the liver and lung, and infusion into the level of the proper hepatic artery was about 5 to 10 times higher in the tumor through the same pixel counts in thin coronal reconstruction image obtained by emission computed tomography.

Assuming all of the radiolabelled Lipiodol accumulated in the tumor for at least a 32 day period, and the effective half life of I-131-Lipiodol is about 6 days, total radiation dose delivered to the tumor is calculated by the equation of

$$D\beta + \gamma = CT (73.8E\beta + 0.0346 P\gamma) \text{ rad}$$

as C: activity of administered I-131

$E\beta$: average energy of Beta emission

T: effective half life

P: gamma factor

For example, if the tumor weight 40 gms, is approximately 5cm in diameter, and one mCi of radioactivity remains in the tumor at least 6 days, the total irradiated tumor dose is about 2,285 rad (22.85 GY) on the lesions with the following assumptions.

$$E\beta : 0.018 \text{ MeV}, T = 6\text{days}, P = 2.18$$

$$D\beta : 1000/40 \times 0.187 \times 6 \times 73.8 = 2,070 \text{ rad}$$

$$D\gamma : 1000/40 \times 6 \times 2.18 \times 19 \times 0.0346 = 215 \text{ rad}$$

$$D\beta + \gamma : 2,070 + 215 = 2,285 \text{ rad}$$

Thus, for a multinodular hepatoma or hypervascular metastatic tumor, if one can deposit one mCi of I-131-Lipiodol on a each vascular tumor measuring 2cm in diameter, the total radiation dose delivered to each tumor will be approximately 28,500 rad (285 GY), which should be sufficient to completely kill the tumor cells.

For a smaller (8cm or less) single lesion, it is feasible to deliver 12,000-20,000 rad (120-200 GY) with I-131-Lipiodol.

For a larger tumor and multifocal lesions, it appears

more effective if one uses a combination of I-131-Lipiodol and gelfoam embolization which is quite effective for the immediate shrinkage of the main tumor mass by occluding the blood supply to the tumor. Safe radiation doses to the liver and lung with internally administered radionuclides are not known, however, the tolerance of external irradiation has been estimated at 30 GY in the liver, and 25 GY in the lung.

Based on these results and MIRD dose calculations, tolerant doses might be 70 mCi in the liver, and 40 mCi in the lung respectively.

The exact mechanism of lung activity is not established. The lipid particles may be small enough to pass through the capillary network of the liver and may be entrapped eventually in the alveolar-capillary spaces of the lungs after conjugation with serum lipoprotein and albumin.

In most of our cases radioactivity in the lung was low; only a few cases showed significant lung activity which was not seen on X-ray films. however, symptomatic pulmonary embolism did not occur, and it was evident that the more prominent the arterio venous shunt on angiography, the more radioactivity was seen both lungs.

In our studies, no instance of hypothyroidism was seen no intestinal symptoms developed which might suggest a possible irradiation effect to the intestine, and no effects either upon the hematologic elements or liver function tests which could be considered an adverse reaction to the administration of radioactive isotope were noted.

Little can be said as to whether treatment increases the life span of the patient, however, a significant number of patients experienced relief of pain, and enjoyed a sense of well-being and increased appetite.

More effective delivery of radiation to the tumor could be applicable using Y-90 (Exam; 2.27 MeV, T1/2:64 Hours, Rmax: 11mm) and P-32 (Exam: 1.17 MeV, T1/2: 14.3 days, Rmax: 8mm) labeled Lipiodol, which would greatly reduce the shielding problem and unnecessary radiation exposure to the surrounding normal tissues by using these non-photon sources. (Ariel 1965; Mantravadi et al. 1982; Mantravadi et al. 1983). Isometric comparison of I-131, Y-90 and P-32 as radiolabels for Lipiodol in the treatment of hepatoma revealed that Y-90 is two times and P-32 six times more effective for the same mCi administration to a tumor. Efforts to label Lipiodol with these pure beta emitters or other elements are now being investigated.

In conclusion, our present finding of selective I-131-Lipiodol deposition in HCC can provide a high

dose of internal radiation delivered to the target tumor and the method appears to be very effective in single massive hypervascular masses less than 8cm in diameter. In addition to the therapeutic benefit, the following is proposed from this study. a) Selective delivery of radiation to target tumor as well as the minor peripheral embolization effect of Lipiodol itself without occlusion of main tumor feeding vessel. b) Ability to demonstrate small daughter nodules. c) Potential value to the accurate determination of size and response of the tumor by serial x-ray examination for a long time period. d) Possible destruction of tumor cells even those multifocal in nature and feasible use for hypervascular metastatic lesions.

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