HIGH-DOSE-RATE AFTERLOADING INTRACAVITARY IRRADIATION AND EXPANDABLE METALLIC BILIARY ENDOPROSTHESIS FOR MALIGNANT BILIARY OBSTRUCTION

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Summary: A double lumen catheter was developed as an applicator for the remote afterloading system (RALS) of ^{60}Co for the intracavitary irradiation of an obstructed common bile duct due to gallbladder cancer in 1 case and by cholangiocarcinoma in 7 cases. This was followed by the biliary endoprosthesis with expandable metallic stents to maintain patency. The mean survival period after treatment was not long (14 weeks). However, removal of the external drainage tube was possible in 7 of the 8 cases, and none of the 8 cases showed dislodgement or deformity of the stent, or obstruction of the bile duct in the stent-inserted area. This combination effectively provided palliation, and has considerable potential for malignant biliary obstruction.

Index Terms

biliary tract cancer, intracavitary irradiation, expandable stent, endoprosthesis

INTRODUCTION

Intracavitary irradiation with a remote afterloading system (RALS) has been used for the treatment of cancer of the uterine cervix and the esophagus. On occasion, malignant biliary obstruction has also been managed by the placement of high-dose-rate iridium wire sources with RALS into a common duct stent[1].

The expandable metallic stent has been devised to dilate stenotic tubular struc-

tures[2)~5)]. It has been successfully employed in patients with vena caval and tracheobronchial stenoses secondary to neoplasms as well as complications of surgery and/or radiation therapy.

The combination of a new applicator for high-dose-rate intracavitary irradiation of ^{60}Co source and expandable metallic stents as a biliary endoprosthesis is described for the treatment of patients with a malignant biliary tract obstruction.

METHODS AND PATIENTS

Applicator (Fig. 1a)

The applicator (Cook Inc., Bloomington, IN) is constructed as a double lumen catheter, 14 Fr outer diameter. One lumen is a blind sac for the insertion of the source of irradiation, while the other allows the insertion of a 0.035 inch guide wire for introduction and exchange.

Technique for insertion

The placement of this applicator is similar to that of any 14 Fr biliary stent. A peel a way catheter can also be used for the insertion.

Irradiation

External irradiation was delivered by a linear accelerator (4MVX) with anterior-posterior parallel opposing portals.

Intracavitary irradiation using high-dose-rate remote afterloading system, RALS, (Ralstron 20B, Shimazu Company, Japan) was performed as follows (Fig. 1b, 1c, 3c): The applicator was exchanged with the external drainage tube. Next a dummy source of radiation was inserted into the applicator to determine the location and distribution of irradiation dosage. Then, with the RALS, a 4 Ci ^{60}Co source which delivers approximately 0.14 Gy/sec at 1 cm was inserted. The irradiation was initiated and moved in intervals of 1 cm.

Expandable metallic stent (Fig. 2a)

The expandable metallic stent is made of a stainless steel wire bent in a zigzag fashion with a certain frequency to make a cylindrical form. A bare stent is prepared by vertically connecting these wires to each other corresponding to the length of the lesion. In addition, a nylon graft prepared by covering a bare stent with cylindrically formed mesh nylon was also used.

Biliary endoprosthesis (Fig. 2b, 3f)

For insertion of the expandable metallic stent, a Teflon introducer and a pusher are used. The introducer is inserted along the guide wire to a position sufficiently beyond the lesion. Then, the inner syringe and the guide wire are removed, and the stent is inserted and advanced through the outer syringe using the pusher. When the tip of the stent has passed the affected area, the pusher is fixed and the outer syringe is slowly removed. If done correctly, the stent gradually leaves the tip of the outer syringe and begins to dilate, resulting in adherence and fixation of the stent to the bile duct wall. At this point, the stent insertion is completed. Subsequently, the outer syringe is exchanged

with an external drainage tube. The patient's condition is observed for about one week of external drainage and after the closure of the external drainage tube, and cholangiography is performed again. After confirming the patency of the bile duct by cholangiography, the external drainage tube is removed and the procedure for biliary endoprosthesis is thereby completed.

Patients Data (Table 1)

Eight cases of advanced biliary tract carcinoma in which obstruction of the extrahepatic bile duct had been seen and surgical treatment had been impossible (7 cases of cholangiocarcinoma and 1 case of gallbladder cancer) were treated. All of them had been diagnosed by cytology and/or diagnostic images (PTC, ERC, CT, US, angiogram etc.) as having malignant biliary obstruction. They consisted of 4 males and 4 females, with ages ranging from 45 to 76 years (mean: 62 years). Total dose of intracavitary irradiation was 30 to 40 Gy, which was delivered in 4 to 6 fractions at twice a week. In seven of these cases, external irradiation at a total dose of 30 to 32 Gy was additionally delivered before and after intracavitary irradiation. All cases received biliary endoprosthesis with an expandable metallic stent within 1 to 2 weeks after irradiation.

RESULTS (Table 1)

In 8 cases, cholangiography was performed via the external drainage tube after intracavitary irradiation. This examination demonstrated that the obstructed bile duct recovered patency (the diameter of the lumen was 5 mm or more) in all of the 8 cases. This finding suggests that the tumor can be locally controlled by intracavitary irradiation. After confirming the recovery of patency in the bile duct, an expandable metallic stent was inserted. After 1 to 2 weeks of external drainage, cholangiography

Table 1. Cases with malignant biliary obstruction

Patient No.	Age(yr)	Sex	Disease	Radiation therapy: Intracavitary* (^{60}Co RALS)	Radiation therapy: External (4MVX or ^{60}Co)	Biliary endoprosthesis	Without external drainage (wk)	Survival (wk)
1	68	F	Gallbladder cancer	37.5/5/15**	32/16/22	Expandable stent	15	Dead 16
2	48	F	Cholangio carcidoma	32.5/5/21	30/15/19	Expandable stent	13	Dead 16
3	70	F	Cholangio carcinoma	40/4/15	32/16/21	Expandable stent	—	Dead 5
4	69	M	Cholangio carcinoma	30/6/22	30/15/22	Expandable stent	11	Dead 21
5	45	M	Cholangio carcinoma	30/6/17	30/15/22	Expandable stent	4	Dead 8
6	57	M	Cholangio carcinoma	30/4/14	—	Expandable stent	17	Alive 18
7	60	F	Cholangio carcinoma	30/4/15	30/15/23	Expandable stent	3	Alive 5
8	76	M	Cholangio carcinoma	30/4/11	30/15/20	Expandable stent	2	Alive 4

* Dose at 10 mm from source ** Dose (Gy)/Fractions/Days

was performed via the external drainage tube. This examination demonstrated no dislodgement of the stent in any case and good passage of the contrast medium.

In 7 of the 8 cases, the external drainage tube could be removed, allowing discharge from the hospital. The maximum duration of complete endoprosthesis has been 17 weeks, which is in the one surviving patient. Even in 4 patients who died, the duration of complete endoprosthesis was 4 to 15 weeks (mean: 11 weeks). None of the cases showed dislodgement or deformity of the stent, or obstruction of the stent-inserted area of the bile duct. Autopsy was performed in 3 cases, in which the lumen of the stent remained patent, and microscopically the area exposed to intracavitary irradiation and the stent-inserted area showed marked fibrosis. Cancer cells were absent in the surface layers of the bile duct wall and/or sporadically seen only in the deep layer. No serious complications was seen in any case.

Case 1 (Fig. 3)

A 68-year-old woman with jaudice due to obstruction of the common duct at the bifurction of the hepatic ducts caused by a gallbladder cancer which infiltrated the right lobe of the liver and the porta hepatis was treated by percutaneous transhepatic external-internal biliary drainage with an 8.3 Fr catheter (Fig. 3a). The patient delivered external irradiation (32 Gy/16 fractions) with a field of 5.0 cm×6.0 cm at a depth of 10 cm. During that period the drainage catheter was gradually dilated up to 14 Fr (Fig. 3b). After external irradiation, intracavitary irradiation was performed five times (twice a week for a total dose of 37.5 Gy) at a distance of 6 cm, in such a manner as to obtain a dose of 7.5 Gy at a site 1 cm from the center of the radiation source (Fig. 3c). After irradiation, a cholangiogram performed through the drainage catheter demonstrated the common bile duct to have a smooth wall and a free flow of contrast material to the duodenum (Fig. 3d).

Three days after the last irradiation, the nylon-covered expandable metallic biliary endoprosthesis (nylon graft) was placed in the common bile duct while the trail stent was located in the common hepatic duct (Fig. 3f). At the time of introduction, the diameter of the stent was 0.7 cm. External drainage was maintained just proximal to the endoprosthesis for four days, at which time it was removed after patency was demonstrated by cholangiography. The stents expanded to 1.1 cm in diameter; the intrahepatic ducts were not dilated; and the passage of contrast medium through the common bile duct into the duodenum was excellent (Fig. 3g, 3h). After the procedure, the patient was free of jaundice and was without complaints. However, sixteen weeks later, the patient died of bile duct bleeding. Postmortem histopathological examination showed no cancer cells in the area exposed to intracavitary irradiation or the stent-inserted area.

Case 2 (Fig. 4)

A 48-year-old woman with the chief complaint of jaudice was performed percutaneous cholangiography which revealed stenosis in the middle to inferior area of the common bile duct (Fig. 4a). Because of marked ascites accompanied by peritonitis carcinomatosa, surgical treatment was impossible in this case.

External irradiation (30 Gy/15 fractions) was performed for the 5×7 cm field at a

depth of 10 cm, using a linear accelerator (4MVX). After external irradiation, intracavitary irradiation was performed five times for a total dose of 32.5 Gy at a distance of 8 cm. After irradiation, a cholangiogram performed through the drainage catheter demonstrated the common bile duct to have a smooth wall and free flow of contrast material to the duodenum (Fig. 4b). One week after irradiation, the expandable metallic biliary endoprosthesis (bare stent) was placed in the common bile duct (Fig. 4c). External drainage was removed after patency was demonstrated by cholangiography. However, sixteen weeks later, peritonitis carcinomatosa worsened and the patient died. Postmortem histopathological examination was performed. Retrograde cholangiogram from the papilla vater of the postmortem specimen demonstrated no obstruction of the stent-inserted area, and the passage to the intrahepatic bile duct was good (Fig. 4d). Macroscopic observation of the cross section showed that the patency of the inner lumen had been kept well, and that the stent wire was embedded in the wall (Fig. 4e). Microscopically, the inner surface of the lumen where the stent had been inserted was found to be covered with thick fibrous tissue; a small number of cancer cells were seen only in the deep layer and no cancer cells were found in the surface layer.

DISCUSSION

At diagnosis most malignant tumors complicated by biliary obstruction are too advanced for radical surgery. Bile duct drainage palliates jaundice but has little effect on the length of survival. External radiation therapy or intra-operative irradiation has not been very effective[6)~8)]. When compared to external irradiation, intracavitary irradiation has the potential to deliver a higher local dose. In the past, low-dose-rate intracavitary irradiation was performed using ^{192}Ir or ^{226}Ra[9)~13)]. For low-dose-rate irradiation which involves long-term insertion of a radiation source, the patient needs to be kept in isolation for a long time. Therefore, a variety of problems (such as exposure of the operator to irradiation, drifting of the radiation source, infection, and physical and mental stess to the patient) can arise. These problems of low-dose-rate irradiation have been solved by ^{60}Co high-dose-rate irradiation with a remote afterloading system[14)]. High-dose-rate intracavitary irradiation has achieved favorable results in patients with cancers of the uterine cervix and the esophagus. Bile duct and pancreatic cancers are less sensitive and should theoretically benefit from intracavitary high-dose-rate irradiation. Encouraging experience with RALS using ^{192}Ir for bile duct cancer has been reported[1)]. This method resembles ours in that it uses an afterloading system and that irradiation can be completed in minutes. However, because the half-life of ^{192}Ir is as short as 74 days, it involves an economic problem that the radiation source has to be frequently renewed. In contrast to ^{192}Ir, ^{60}Co has a long half-life (about 5 years); therefore, it can be used for many patients. This is an economic advantage.

The conventional applicator designed for RALS using ^{60}Co has a blind sac requiring a tube with an internal diameter of at least 4 mm and an outside diameter of 5 mm. The insertion of such a large tube into the bile duct through a sheath is technically more

difficult. Our newly developed double lumen applicator described in this presentation has an external diameter of 5 mm, 14 Fr, one lumen accepts a 0.035 inch wire for easier insertion. This also allows ready exchange with a smaller drainage tube.

The expandable metallic stents were devised by Gianturco and reported by Wright[2] et al. They have been successfully used in laboratory animals with a normal biliary duct and tracheobronchial tree, normal and stenosed vascular system, as well as in patients with stenoses of the vena cava, trachea, and bronchus[3]~[5]. Its clinical application in the biliary tract has considerable potential. Biliary endoprosthesis is advantageous in that it involves a low risk of infections and that it allows the patients to bathe and to restore their social activity. However, the problems involved in endoprosthesis (such as obstruction or dislodgement of the internal drainage tube) have not been solved yet[15][16]. To reduce the obstruction of the internal drainage tube, a tube of larger diameter (12 Fr or more) is necessary[17]. However, insertion of such a large diameter tube causes much stress to the patient and elevates the risk of complications. Expandable metallic biliary endoprosthesis can solve this problem, because the biliary tract can be kept patent using an introducer with a small diameter. The stent used for this technique is capable of self-expanding; therefore, it prevents the growth of tumor and delays reobstruction. Furthermore, it involves hardly any risk of dislodgement. It is possible to insert another stent through the lumen of a stent for the purpose of increasing expandable power and also perform endoprosthesis of multiple intrahepatic branches. As seen in the microscopic examination of autopsied Case 2, the bile duct kept its patency in spite of marked fibrosis in the bile duct wall. In addition, because the stent wire is embedded in the fibrous tissue of the wall, it is unlikely that biliary stasis (for which the stent serves as a core) and the subsequent cholangitis occur. Our clinical experience with this technique in 8 cases of biliary tract cancer indicates that intracavitary irradiation combined with external irradiation can locally control the tumor; that biliary endoprosthesis with an expandable metallic stent works to keep the bile duct patent by preventing the tumor regrowth and the reobstruction due to radiation fibrosis and therefore prevents fatal obstruction of the common bile duct and allows discharge of the patient in a short period; and that the combination of high-dose-rate intracavitary irradiation and expandable metallic biliary endoprosthesis is the most excellent combination therapy currently available from the viewpoint of the quality of life. Trial applications of this combination therapy have only just recently begun; therefore, there are many unsolved problems. Furthermore, to ensure long-term control of malignant biliary obstruction with this therapy, we have to try it in more cases for obtaining the optimal total dose and fraction time of intracavitary irradiation and optimal dose allotment in intracavitary and external irradiation, and assessing the effect of long-term insertion of an expandable stent on the bile duct. Because this therapy appears very promising for the treatment of inoperable malignant biliary tumors, we plan to use it as first choice from now on.

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Legends

Fig. 1. a: A newly developed applicator for RALS, which has a double lumen, allows insertion of a 0.035 inch wire and easy exchange with a drainage tube (arrow). A 4 ci dummy source of ^{60}Co (arrowhead).

b: Picture of a patient irradiated with RALS. A ^{60}Co source is inserted to the tumor-affected area using the remote afterloading system. Irradiation takes only a few minutes.

c: Procedure and technique of intracavitary irradiation with ^{60}Co. i) External and internal drainage are performed, and the lumen is dilated up to 14 Fr diameter. ii) Using a 0.035 inch guide wire, the drainage tube is exchanged with a RALS applicator. iii) For the simulation, a dummy radiation source is inserted, and the region for irradiation is decided. iv) With the remote afterloading system, intracavitary irradiation is performed moving a ^{60}Co radiation source at an interval of 1 cm.

Fig. 2. a: Expandable metallic stent.
*=Bare stent, **=Nylon graft

b: Procedure and technique of expandable biliary endoprosthesis. i) The introducer is inserted along the guide wire to a position sufficiently beyond the lesion. ii) The inner syringe and the guide wire are removed, and the stent is inserted and advanced through the outer syringe using the pusher. iii) When the tip of the stent has arrived at the lesion, the pusher is fixed and the outer syringe is slowly removed. If done correctly, the stent leaves the tip of the outer syringe and begins to dilate. iv) After all stents have left the tip of the outer syringe and have been dilated, the outer syringe is exchanged with an external drainage tube. After one-week follow-up observation and confirmation of patency, the external drainage tube is removed to complete the procedure of endoprosthesis.

Fig. 3. Case 1: A 68-year-old woman with gallbladder cancer.

a: Percutaneous cholangiogram showed complete obstruction of the bile duct at the porta hepatis.

b: External-internal drainage and dilatation of the tract to 14 Fr in diameter.

c: With the guidance of a 0.035 inch wire, the drainage catheter was exchanged for the applicator of RALS, and then intracavitary irradiation was performed with movement of the radiation source at 1 cm intervals.

d: Three days after irradiation, a cholangiogram revealed the common bile duct to be patent with good drainage into the duodenum.

e: The isodose distribution of intracavitary irradiation demonstrated on CT showed a high localized dose distribution in the tumor area.

f: Three days after irradiation a nylon-covered expandable metallic biliary endoprosthesis (nylon graft) was inserted into the common bile duct through a 12 Fr introducer. Cholangiogram opacified the common bile duct through the expandable stents.

g: One month after placement of expandable stent, there was good expansion without the deformity and the dislodgement of expandable stent.

h: Two months after placement of expandable stent, CT showed marked improvement

with maintenance of patency of the common bile duct.

Fig. 4. Case 2: A 48-year-old woman with cholangiocarcinoma.

a: The first PTC. Irregular stenosis is seen in the middle to inferior area of the common bile duct.

b: A cholangiogram from the external drainage tube after irradiation. The bile duct wall is smooth, and passage is good.

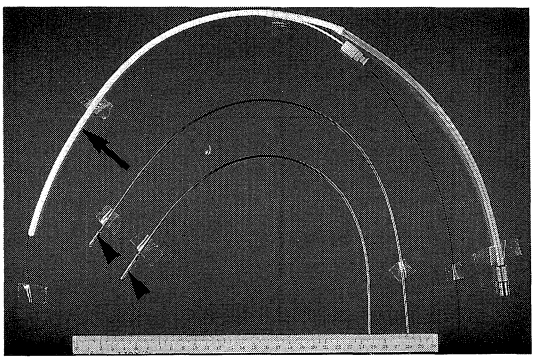
c: One week after irradiation an expandable biliary endoprosthesis was inserted. Cholangiogram demonstrated the good passage of the common bile duct through the expandable stent.

d: Autopsy specimen. Retrograde cholangiogram from the papilla vater demonstrated the patency of the stent-inserted area and good passage to the intrahepatic bile duct.

e: Macroscopic observation of the cross section. The patency of the bile duct is kept. The stent wire is not seen on the surface, it is embedded in the wall.

f: Microscopic observation. The inner surface of the duct where the stent was inserted is covered with thick fibrous tissue. No cancer cells are seen on the surface.

*=Cavities where the stent wires were located.



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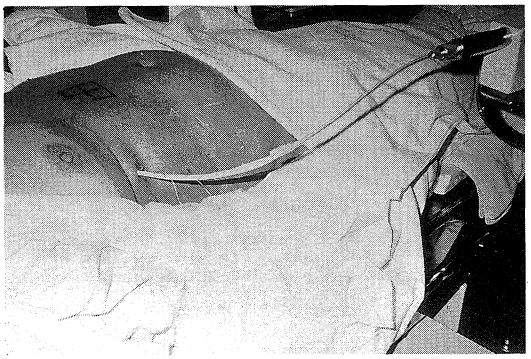

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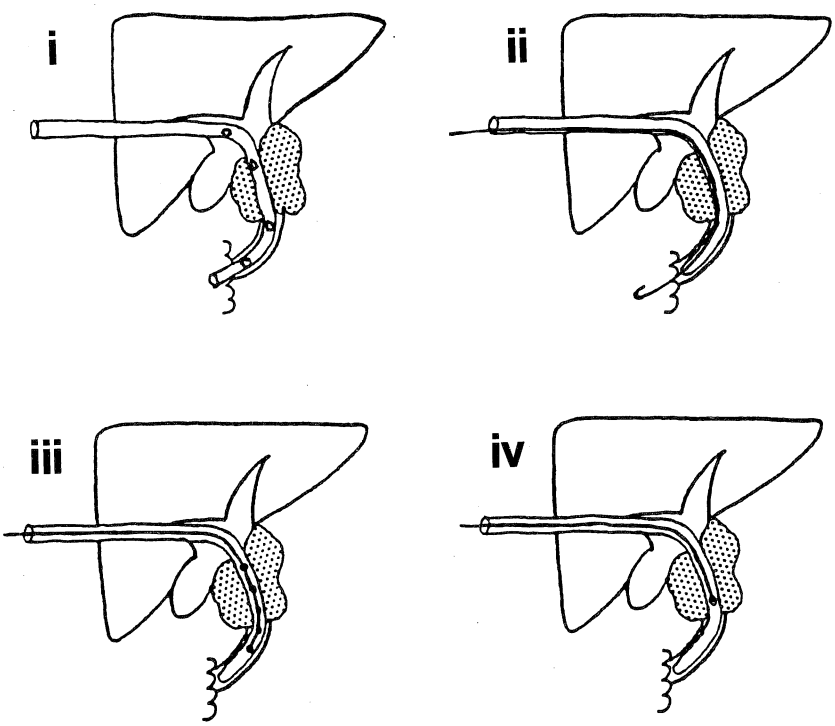

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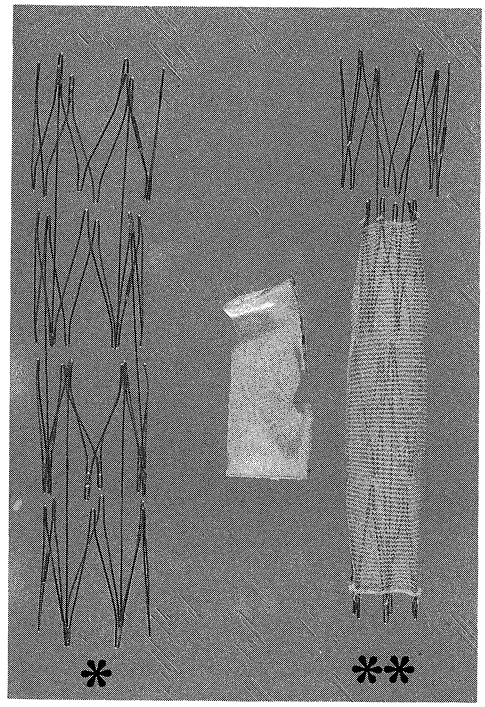

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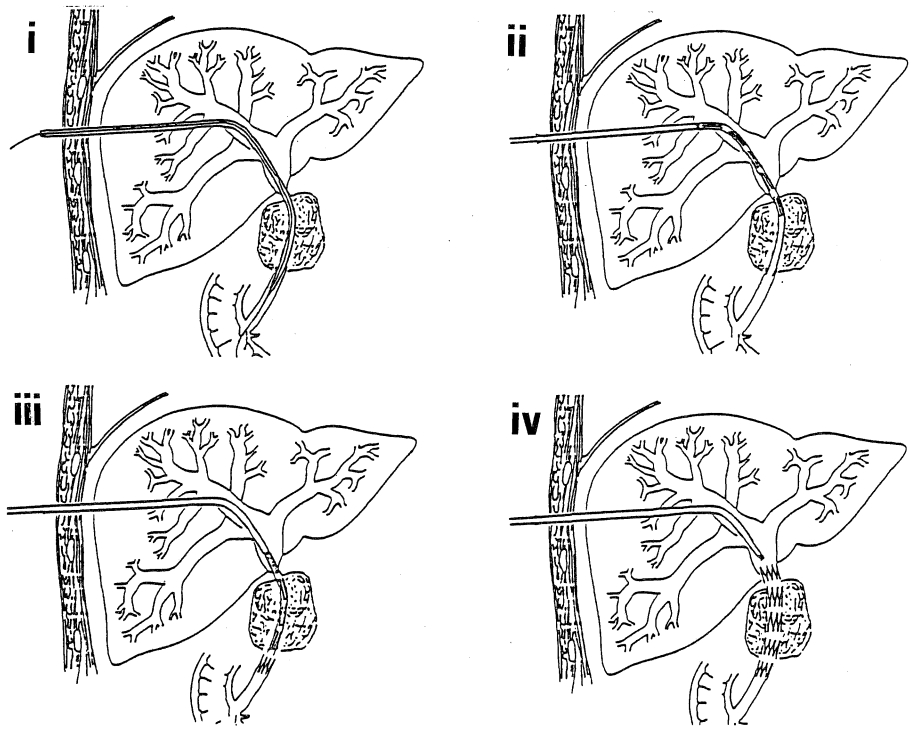

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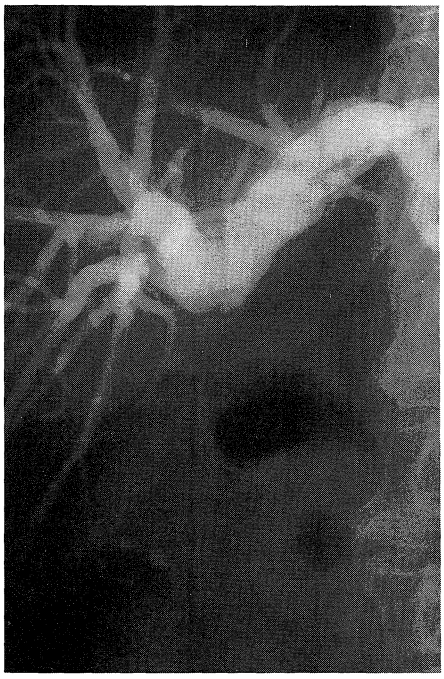

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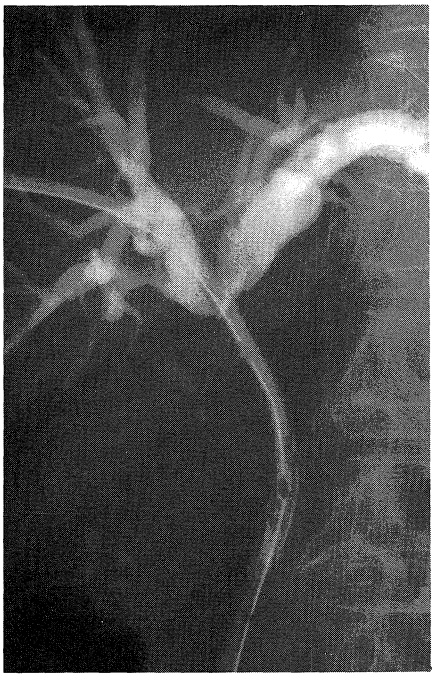

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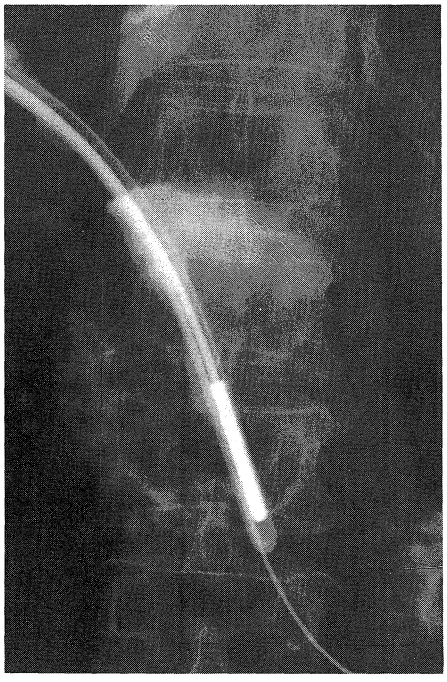

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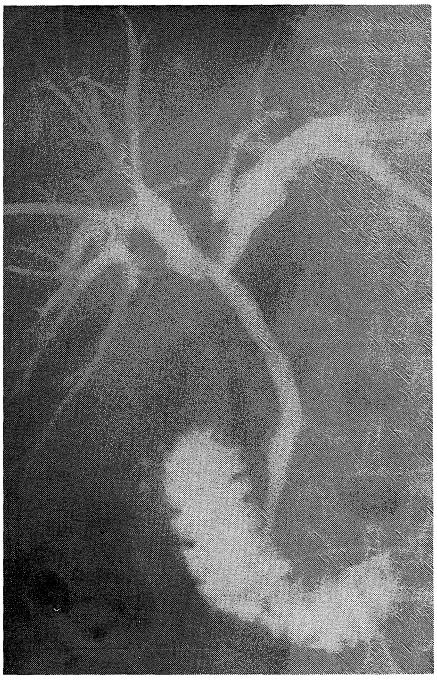

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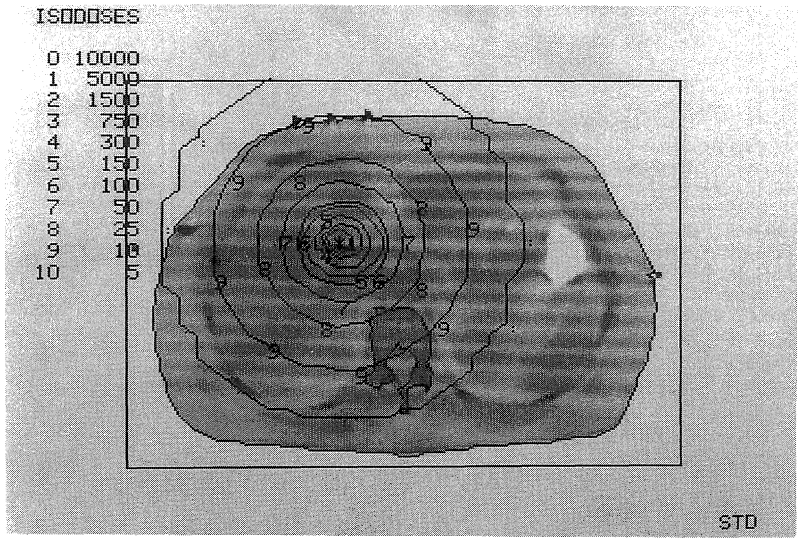
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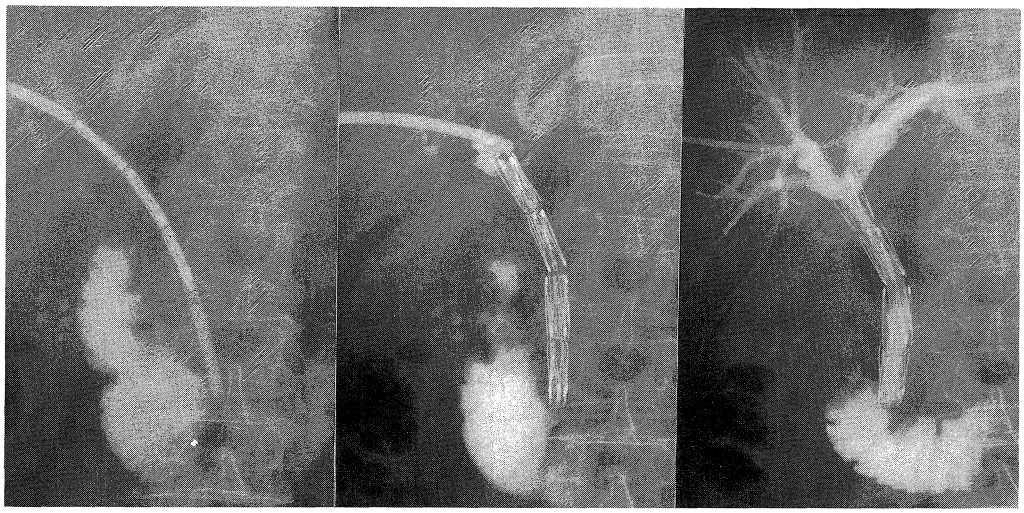

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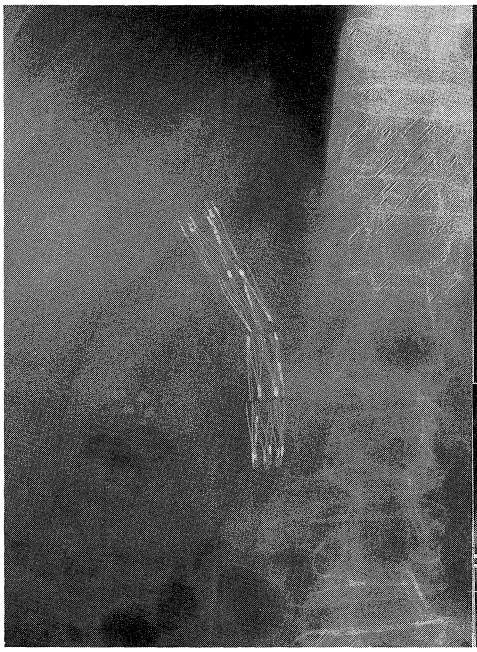

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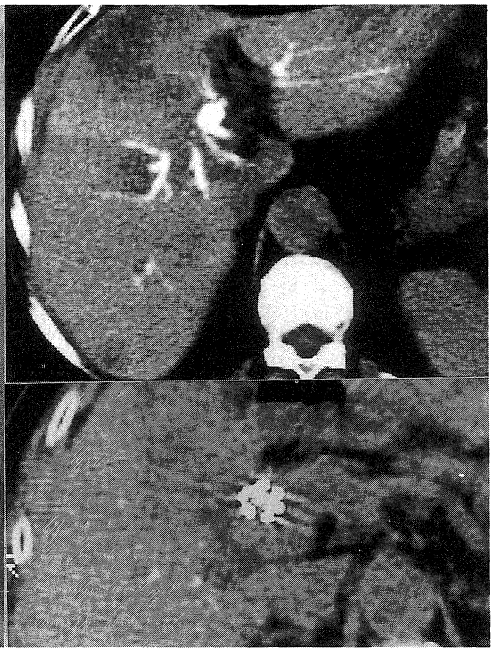

Fig. 3. h

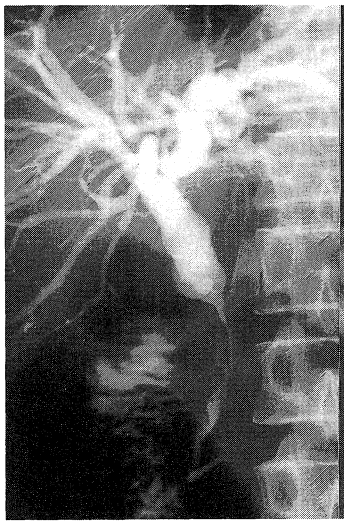

Fig. 4. a

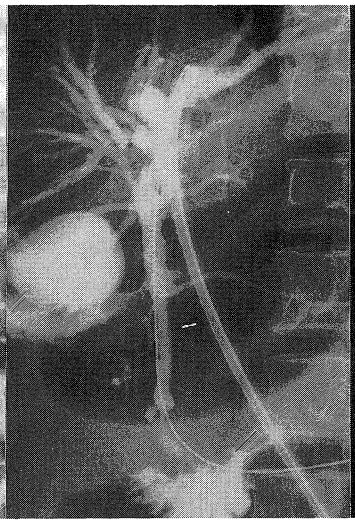

Fig. 4. b

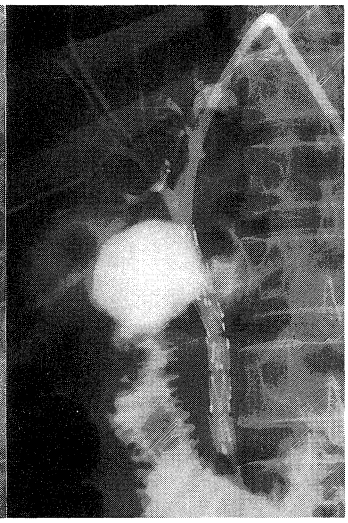

Fig. 4. c

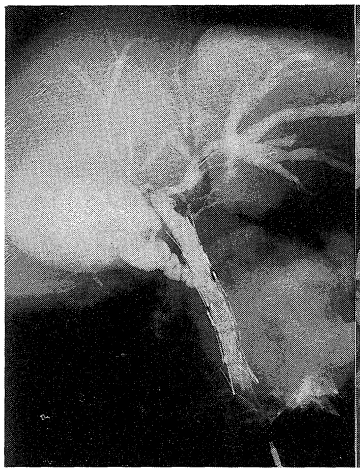

Fig. 4. d

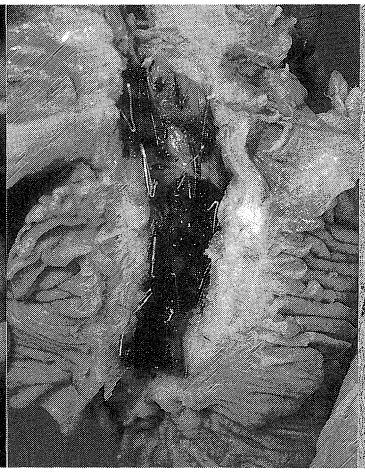

Fig. 4. e

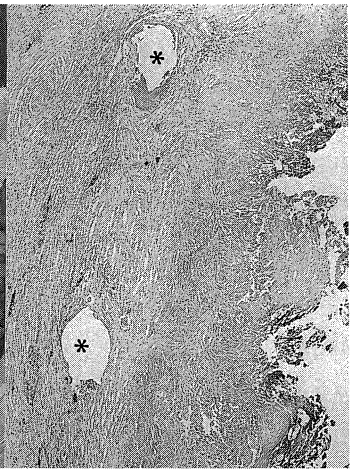

Fig. 4. f