Acta Radiologica: Therapy, Physics, Biology

ISSN: 0567-8064 (Print) (Online) Journal homepage: informahealthcare.com/journals/ionc17

Intra-Operative Irradiation in Abdominal and Cerebral Tumours

M. Abe, M. Fukuda, K. Yamano, S. Matsuda & H. Handa

To cite this article: M. Abe, M. Fukuda, K. Yamano, S. Matsuda & H. Handa (1971) Intra-Operative Irradiation in Abdominal and Cerebral Tumours, Acta Radiologica: Therapy, Physics, Biology, 10:4, 408-416, DOI: 10.3109/02841867109130786

To link to this article: https://doi.org/10.3109/02841867109130786

FROM THE DEPARTMENTS OF RADIOLOGY AND NEUROSURGERY AND THE SECOND DIVISION OF SURGERY, FACULTY OF MEDICINE, KYOTO UNIVERSITY, JAPAN.

INTRA-OPERATIVE IRRADIATION IN ABDOMINAL AND CEREBRAL TUMOURS

by

M. ABE, M. FUKUDA, K. YAMANO, S. MATSUDA and H. HANDA

Radiotherapy is rarely employed for abdominal neoplasms in adults since these are mostly radioresistant adenocarcinomas and external irradiation to the abdomen inevitably causes intestinal damage. Surgery has therefore been preferred either for curative or palliative purposes for practically all abdominal tumours. Recent developments in anesthesia and antibiotics have also assisted in this choice although the elimination of cancer nests around major blood vessels is still well-nigh impossible. Microscopic lesions may remain even if the operation is considered radical. The problems obviously cannot be resolved by surgery alone.

'Intra-operative irradiation' has therefore been developed. The resectable lesions are treated by surgery and the remaining malignant remnants sterilized by irradiation with a single massive dose during the operation (2, 3, 9, 12). This method has two advantages. First, an adequate field may be determined with accuracy under direct vision, otherwise impossible to achieve. Secondly, since normal organs adjacent to the tumour may be moved from the field so that the lesion to be irradiated may be exposed directly to radiation any damage to the

Submitted for publication 16 July 1970.

Fig. 1. Intra-operative irradiation to carcinoma of the stomach with an electron beam.

normal structures is minimized. These advantages made it possible to deliver a sufficient dose to the abdominal neoplasm without affecting the small intestine.

This type of radiotherapy demands however that the largest possible dose administered at one session to the tumour area must be smaller than the tolerance dose of normal critical organs that cannot be moved from the field. Any possible success with radiotherapy depends of course upon a safe ratio or differential between the dose delivered to the new growth and that to the normal tissue. The cancerocidal dose is generally agreed to be about 6 000 R in the case of fractionated irradiation, but there is little information available for determining the equivalent single dose for intra-operative irradiation (4, 7, 13). From data published on intra-operative irradiation (5, 6, 8, 10, 11) and the authors' fundamental experiment (1), it was estimated that 2 500 to 4 000 R may be a single dose equivalent to 6 000 R given fractionately. This new radiotherapy has been applied mostly in cases where surgery cannot remove the primary growth in the abdomen, its local spread and regional lymph node metastases.

Method. The irradiation is planned and executed by a team of radiologists and surgeons. The operation is performed most conveniently in an irradiation room. With no betatron and the intra-operative irradiation carried out with ^{60}Co, the patient is moved under general anesthesia from an operation theatre to the ^{60}Co room. A betatron was, however, eventually installed in a theatre in which the operation could also be performed. Irradiation in carcinoma of the stomach usually took place following the gastrectomy and before the suturing because, at this stage, the site to be irradiated can be adequately exposed and the organs to be protected pulled aside. Careful control of the general anesthesia is necessary during the irradiation to prevent movement, the condition of the patient being observed by a distant monitoring system. Fig. 1 depicts intra-operative irradiation with an electron beam in a patient with carcinoma of the stomach.

Case reports and Results

Carcinoma of the pancreas. Two cases were treated but only one could be followed.

Illustrative case. Female, aged 75, with carcinoma of the head of the pancreas was the first to be treated with intra-operative irradiation. When admitted, she was jaundiced and had a large firm mass in the upper abdomen. Laparotomy revealed that it was about 5 cm in size and lay in the head of the pancreas with lymph node metastases extending into the duodenum; the gallbladder was distended. The tumour was considered inoperable. After choledocho-jejunostomy, a single dose of 2 500 R was delivered from a ^{60}Co source to the surface of the main mass through a 5.8 cm×3.6 cm field. The stomach and small intestine were retracted from the field with stay sutures and the region tightly packed with towels. Jaundice disappeared within a few weeks while the abdominal mass regressed and was not palpable at the time of discharge 30 days after the irradiation. The patient had no symptoms for about 200 days until she again developed nausea and vomiting. Further laparotomy 31 weeks after the first irradiation disclosed that the mass was reduced to about a third of the size recorded at the first irradiation. Preceding gastro-jejunostomy, a second intra-operative irradiation, this time with 2 000 R, was applied to the main mass, including the infiltrated duodenum, through a 4 cm×4 cm field. Although the post-operative course was smooth the patient died suddenly of cerebral hemorrhage seven days after the second irradiation. Histologic examination of the irradiated main tumour disclosed an adenocarcinoma with a few cells in a dense fibrous stroma. Concern had been felt about perforation of, or bleeding from the exposed duodenum, but a marked regeneration of the intestinal villi occurred and no complications were evident throughout the survival period. Autopsy revealed small metastases in the liver, lungs, skeleton and kidneys.

Carcinoma of the biliary system. Three patients were treated. Marked regression was evident at autopsy in 2 of these and at exploratory laparotomy in the other.

Illustrative case. Female, aged 58, with a large mass, about 8 cm in diameter, in the right infra-hepatic region and invading the adjacent liver with numerous lymph node metastases around the common hepatic artery at laparotomy. The growth was diagnosed as carcinoma of the gallbladder and considered inoperable. A single dose of 2 500 R 18 MeV electron radiation was given through a 10 cm×10 cm field (Fig. 2). A T-tube was inserted through the common bile duct in order to prevent obstructive jaundice, a procedure followed by partial gastrectomy. The patient tolerated the procedure well and recovered satisfactorily. A large amount of muddy discharge, consisting of tissue debris, was drained via the tube at the tenth post-irradiation day and at the same time a significant elevation of the serum transaminase was recorded. Three weeks later the mass in the right upper abdomen disappeared. Two months after irradiation a rise in temperature suggesting a peritoneal abscess led to a second laparotomy. This revealed marked regression of the mass. The primary tumour and the hepatic metastases had become a cyst about 5 cm in size, with a smooth surface and containing serous pus and encapsuled by firm scar tissue. The cyst was evacuated, and for the purpose of intra-arterial infusion chemotherapy, a teflon tube was inserted into the common hepatic artery. A total of 4 500 mg 5FU was continuously infused via the catheter for three weeks. The patient had no symptoms or signs four months after intra-operative irradiation. Histologic comparison of the biopsy specimens obtained at both operations indicated a definite carcinostatic effect from the irradiation.

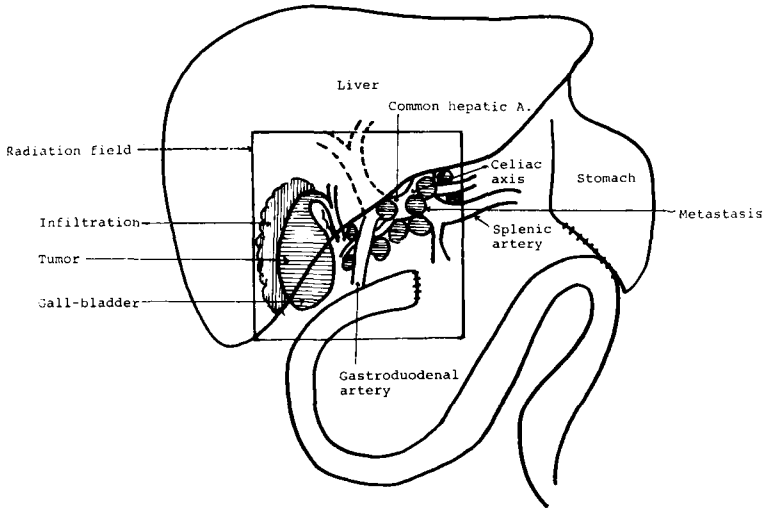

Fig. 2. Field localization in a patient with carcinoma of the gallbladder.

Carcinoma of the stomach. Twenty-nine patients with carcinoma of the stomach were treated with intra-operative irradiation. The patients were divided into three groups.

Group 1. Patients (five) in an advanced stage who received only exploratory laparotomy or shunt operation. Intra-operative irradiation was administered to patients in this group to alleviate symptoms and prolong life. Doses ranging from 1 800 to 3 000 R from a ^{60}Co source were delivered to the tumour during laparotomy in 4 patients and 4 000 R with 20 MeV electrons in one patient. The effect of a single dose of 1 800 R was not apparent, but remission of stenosis from large masses was obtained about two weeks after exposure in 4 patients who received more than 2 000 R.

Illustrative case. Female, aged 30, with inoperable carcinoma of the stomach, was admitted complaining of difficulty in swallowing any kind of solid or semi-solid food. Laparotomy revealed carcinoma of the cardia infiltrating the entire stomach. The proximal gastric segment was irradiated with a single dose of 3 000 R and gastrostomy was performed for tube feeding. There was marked improvement in the stenosis, beginning as early as the second week after the exposure and continuing until the patient died with general metastases on the 114th day following irradiation.

Group 2. Patients (sixteen) with malignant remnants as a result of incomplete excision of neoplasms. This group is the most suitable for intra-operative irradiation. An attempt was made to sterilize with radiation the lesions that usually remain in the infrahepatic region, including the porta hepatis, the celiac trunk

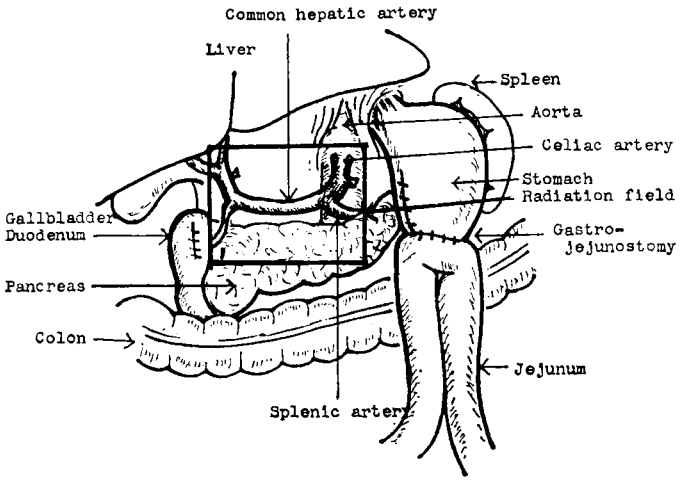

Fig. 3. Carcinoma of the stomach. The primary growth may be removed but metastases around vessels such as the celiac artery and portal vein may persist. Diagram of field localization used.

and its main branches as well as the para-aortic region. Fig. 3 depicts the radiation field. Five out of 16 patients survived more than a year and 2 patients are still alive, one after 27 months and one patient after 36 months; both have returned to work with no evidence of recurrence.

Group 3. Patients (eight) who underwent radical operation. An increase in the cure rate can be obtained only when microscopic lesions are eliminated. Intra-operative irradiation was administered to 8 patients who had had a radical operation. Three patients survived more than a year, one patient for two and half years, and one patient lived for three years without symptoms.

Carcinoma of the colon and retroperitoneal tumours. Intra-operative irradiation was given to 6 patients with carcinoma of the colon, and to one with recurrent carcinoma of the corpus uteri and with peritoneal reticulosarcoma. Two patients with growths of the caecum and one with a neoplasm of the sigmoid colon are alive, 2 of them with no sign of recurrence for three years.

Illustrative case. Male, aged 63, who had undergone right hemicolectomy for carcinoma of the colon five years previously, was admitted with abdominal distension and increasing pain in the back. Laparotomy revealed a recurrence near the terminal ileum which was about 5 cm in diameter and infiltrated the right iliac fossa and the nerve plexus. The main tumour was removed, but a large mass around the nerve plexus and the inferior vena cava, was irradiated with 3 000 R ^{60}Co preceding colonic anastomosis. Histology revealed colloid carcinoma. Recovery was complete for about ten months until the patient again began to complain of epigastric pain and had a massive hematemesis. Further laparotomy revealed no obvious malignant lesion at the irradiated site. The patient died of hepatitis induced by surgery 307 days after irradiation.

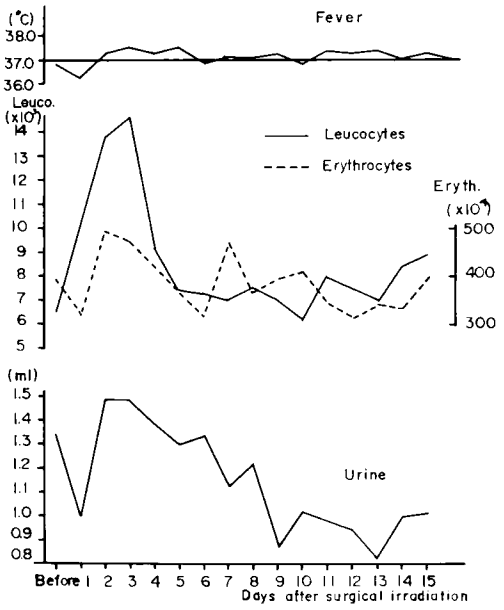

Fig. 4. Changes in urine volume, temperature and blood cell counts after intra-operative irradiation in 29 patients with carcinoma of the stomach.

Cerebral tumours. Intra-operative irradiation was administered to 2 patients with recurrent cerebral tumours who had once received a course of conventional post-operative radiotherapy.

Illustrative cases. Female, aged 57, with an occipital tumour, who had received 5 960 R from a ^{60}Co source after partial resection of a growth that was histologically a fibrosarcoma. She was well for 8 months until she again developed hemiparesis and ataxia. Further craniotomy disclosed a 5 cm recurrent tumour with invasion of the surrounding structures 3 cm below the dura. The lesion was partly removed and a single dose of 3 500 R 18 MeV delivered through a 8 cm field. The post-operative course was smooth and uneventful. The patient was almost free from symptoms and signs for 5 months until she again developed ataxia and died 189 days after the irradiation.

Female, aged 37, with vertigo and anorexia. A tumour in the right frontal region, diagnosed as a glioblastoma was partly resected and 5 940 R from a ^{60}Co source given fractionately. Progression of the disease necessitated recraniotomy which disclosed an undemarcated mass in the frontotemporal region. After partial resection, a single dose of 4 000 R of 12 MeV electron energy was administered to the main lesion through a 4 cm field. The post-operative course was uneventful until the patient became febrile 2 months later. Probable radiation-induced necrosis indicated craniotomy on the 63rd post-irradiation day, in which the irradiated region contained only necrotic tissues; the temperature fell to normal after aspiration of the necrotic mass. The patient again became febrile 2 weeks later and died on the 87th day following the irradiation. Autopsy could not be performed.

Fig. 5. Percentage depth dose distribution of 18 MeV electron beam through an 8 cm field.

Complications. Almost all patients recovered without serious complications or deviations from the usual post-operative course. Wound healing, recovery of appetite and bowel function were not disturbed. The urine, blood cell count and blood chemistry including S-GOT, S-GPT, alkaline and acid phosphatase bilirubin, blood urea nitrogen and protein fractions were frequently examined but no definite changes attributable to irradiation were apparent. Fig. 4 presents mean values of urine volume, fever, blood cell counts before and after intra-operative irradiation in 29 patients with carcinoma of the stomach. Exposure of the second part of the duodenum cannot be avoided in intra-operative radiotherapy for carcinoma of the head of the pancreas. Concern was therefore felt for possible perforation of or bleeding from this region; no such sequelae occurred however in the 2 000 to 2 500 R dose range. The symptoms of 29 patients with carcinoma of the stomach were within tolerable limits following irradiation (Table).

Discussion

An electron beam with a sharp and rapid fall-off in depth dose offers the particular advantage of minimizing the exposure of normal tissues located under tumours. Fig. 5 shows a depth dose distribution of irradiation with 18 MeV electrons. An 80 per cent dose range down to the depth of the celiac artery leaves the bone marrow almost free from exposure. A sterilising dose can there-

Table

Symptoms (in per cent) of 29 patients with carcinoma of the stomach after intra-operative irradiation

	Be-	Days after intra-operative irradiation													
	fore	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Nausea	9.1	13.8	18.1	9.1	0	0	0	0	0	0	0	0	4.6	4.6	4.6	9.1
Vomiting	0	4.6	4.6	9.1	0	0	0	0	0	0	0	0	4.6	4.6	4.6	4.6
Vertigo	4.6	0	4.6	4.6	0	0	0	0	0	0	0	0	0	0	0	0
Anorexia	27.3	27.3	27.3	27.3	22.7	22.7	18.1	18.1	9.1	18.1	22.7	22.7	18.1	22.7	18.1	9.1
Insomnia	0	13.8	13.8	9.1	9.1	9.1	9.1	4.6	0	0	0	0	0	0	0	0
Fatigue	9.1	22.7	13.8	18.1	22.7	18.1	13.8	9.1	4.6	4.6	9.1	9.1	9.1	9.1	13.8	18.1
Pain	13.8	13.8	9.1	9.1	4.6	4.6	0	0	0	0	0	0	0	0	0	0
Diarrhea	0	0	0	0	4.6	0	0	0	0	0	0	0	0	0	0	0
Hematemesis	0	0	0	0	0	0	0	0	0	0	0	0	4.6	4.6	9.1	9.1
Melena	0	0	0	0	0	0	0	0	0	0	0	0	4.6	4.6	9.1	9.1

fore be delivered to the lesion with a sharp limitation of the total volume of tissue included in the high dose range. This characteristic may also be favourable for the treatment of cerebral tumours, in which lesions are removed by operation and the remnants eliminated by direct exposure to an electron beam.

The number of patients treated by this method is insufficient and the follow-up period too short for a definite evaluation to be made. It is assumed that a single dose of at least 2 500 R is necessary as a cancerocidal dose for adenocarcinoma. Intra-operative irradiation to abdominal tumours produces no harmful complications, such as perforation of or bleeding from the intestine, diarrhea, anorexia or abdominal pain at a dosage less than 4 000 R measured at the surface of the tumour. Long-term survival may be expected following intra-operative irradiation to localized small remnants or possible lesions that remain after operable lesions.

SUMMARY

A method of 'intra-operative irradiation' for the treatment of abdominal neoplasms is described. This consists in the irradiation of primary growths and malignant remnants during the course of ordinary radical surgery. The method appears to possess many advantages and the preliminary results seem most encouraging.

ZUSAMMENFASSUNG

Eine Methode für die intraoperative Bestrahlung von malignen Bauchtumoren nach operativer Freilegung wird beschrieben. Die Methode scheint mehrere Vorteile zu bieten und die vorläufigen Resultate erscheinen versprechend.

RÉSUMÉ

Description d'une méthode d'irradiation per-opératoire pour le traitement des tumeurs abdominales. Elle consiste en l'irradiation des tumeurs primitives et des parties malignes restantes au cours d'une intervention chirurgicale radicale ordinaire. Cette méthode paraît avoir de nombreux avantages et les résultats préliminaires semblent très encourageants.

REFERENCES

1. Abe M. and Arakawa M.: Fundamental studies on surgical irradiation. Histological and hematological changes followed by irradiation during laparotomy of dogs. J. Jap. Cancer Th. 2 (1967), 271.
2. — Yamano K. and Matsuda S.: Intraoperative radiotherapy of abdominal tumors. Part III. Intraoperative irradiation to carcinoma of the colon and retroperitoneal tumors. Nipp. Acta. radiol. 29 (1970), 1488.
3. — — Imura T. and Matsuda S.: Intraoperative radiotherapy of abdominal tumors. Part I. Intraoperative irradiation to carcinoma of the pancreas head and biliary system. Nipp. Acta. radiol. 29 (1969), 75.
4. Andrews J. R. and Moody J. M.: The dose-time relationship in radiotherapy. Amer. J. Roentgenol. 75 (1956), 590.
5. Barth G.: Erfahrungen und Ergebnisse mit der Nahbestrahlung operativ freigelegter Tumoren. Strahlentherapie 91 (1953), 481.
6. — und Meinel F.: Intraoperative Kontakttherapie in den grossen Körperhöhlen. Strahlentherapie 109 (1959), 386.
7. Fowler J. F. and Stern B. E.: Dose-rate effects: Some theoretical and practical considerations. Brit. J. Radiol. 33 (1960), 389.
8. Fucks G. und Ueberall R.: Die intraoperative Röntgentherapie des Blasen-Karzinoms. Strahlentherapie 135 (1968), 280.
9. Fukuda M., Abe M., Yamano K. and Matsuda S.: Intraoperative radiotherapy of abdominal tumors. Part II. Intraoperative irradiation to carcinoma of the stomach. Nipp. Acta. radiol. 29 (1969), 390.
10. Goin L. E. and Hoffman E. F.: The use of intravesical low-voltage contact roentgen irradiation in cancer of the bladder. Radiology 37 (1941), 545.
11. Lutterbeck E. F.: Contact roentgen radiation of bladder tumors. J. Urol. 82 (1959), 90.
12. Matsuda S., Satomura K., Yamane M. et coll.: Clinical study on surgical radiation therapy for advanced abdominal cancer. J. Jap. Cancer Th. 2 (1967), 279.
13. Strandqvist M.: Studien über die kumulative Wirkung der Röntgenstrahlen bei Fraktionierung. Acta radiol. (1944) Suppl. No. 55.