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Correspondence address
Radiology and Oncology
Institute of Oncology
Vrazov trg 4
61000 Ljubljana
Slovenia

Phone: + 38 61 314 970
Fax: + 38 61 329 177

Reader for English language
Olga Shrestha

Design
Monika Fink-Serša

Key words und UDC
Eva Klemenčič

Secretaries
Milica Harisch
Betka Savski

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Radiological aspect of peptic ulcus relapse following vagotomy and pyloroplasty

Milivoj Dujmović, Ivan Lovasić, Milan Prica, Milan Radić

Clinical Hospital Center Rijeka, Institute of Radiology, Clinic of Internal Medicine Health Center Krk, Croatia

Changed anatomic relations in pylorobulbar area with altered contour appearances and unusual course of folds are the causes of pseudocicatricial changes and the ulcer niches and craters, conditioning great difficulties in discovering of peptic ulcus relapse. Indirect relapse signs are of much greater significance during radiological examinations. The finding of stenosis, especially accompanied by other indirect relapse signs and clinical symptoms, represents a reliable sign of the repeated appearance of peptic ulcer. In our group of examined patients relapses were found by radiological method in 3.74 % of cases and by endoscopic method in 7.35 % of cases. The preference has been given to the endoscopic examination, especially at ulcus discovered in a deformed pylorobulbar area. Conversely, radiological examination is indispensable in evalution of stomach emptying, and the presentation of the site, level and length of stenosis. Radiological examination offers us better possibilities in verifying of complicated ulcus relapse than the endoscopic examination.

Key words: peptic ulcer-radiology; vagotomy; pylorus-surgery; recurrence

Introduction

Changed anatomic relations in pylorobulbar area are the cause of great difficulties in radiological interpretation of a peptic ulcus relapse. Data about the relapse frequency cited in literature vary very much, depending on the kind of vagotomy, the drainage method and the postoperative time.

Proximal selective vagotomy (PSV) with drainage operation or without it should be followed by the least number of relapses.[1–3] Various percentage of relapses concerning the total posterior vagotomy combined with the selective anterior vagotomy, partially time dependent as well, have been reported in literature, ranging from 2.4 % to 10 %. The percentage of relapse exceeds 20 % at bilateral total vagotomy.[4–8]

Various relapse percentages are also reported in literature with reference to particular types of drainage operations, ranging from 20–27 % at vagotomy and gastroanastomosis to 22.5 % at vagotomy combined with Heineke-Mikulicz pyloroplasty, and 10.9 % after Finney's pyloroplasty.[2, 3, 6, 9] Clinical data referring to the same group of examined patients, being the topic of our study but during a much earlier treatment phase, speak about 2.4 % of relapses at Hei-

Correspondence to: Doc. dr. sc. Dujmović Milivoj, Kliničko bolnički centar Rijeka, Zavod za radiologiju, 51000 Rijeka, Krešimirova 42, Croatia.

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neke-Mikulicz pyloroplasty and no relapses after Finney's pyloroplasty.[4, 5]

According to literature, relapse occurrences are most frequently expressed during the first postoperative year (80 %). Their number increases up to the tenth year following surgery.[4, 5, 7]

The purpose of this paper is to establish the real place of radiological diagnostics in peptic ulcus verification following vagotomy and pyloroplasty, with special emphasis on the endoscopic method of examination. We tried to evaluate particular radiological relapse symptoms and to draw a parallel between the relapse frequency and literature quotations based on a long-term follow-up of the patients.

Patients and methods

Because of ulcus disease, from January 1st 1965 to the end of 1984 1358 patients underwent vagotomy using one of drainage methods. Anterior selective vagotomy (VSA) and total posterior vagotomy (VTP) were performed as a rule. Urgent and adipose older patients underwent bilateral total vagotomy (VTA and VTP).[4, 5, 7, 10, 11]

Of drainage operations, sec. Finney was applied 1230 times (90 %) and sec. Heineke-Mikulicz (in the earliest phase) 104 times (8 %).[4, 5, 7, 10, 11]

VSA and VTP were most frequently performed in combination with Finney's pyloroplasty – 991 times (74 %), whereas VTA and VTP combination with sec. Finney took the second place by being used 249 times (18 %). VTA and VTP with Heineke-Mikulicz pyloroplasty was carried out 96 times (7 %) at the initial use of the method.

The number of male operated patients amounted to 1154 (85 %), vs. 204 (15 %) in females. Most of the operated males were in the fourth and fifth and females in the fifth and sixth life decade.

The sequence of indications for surgery in our group of patients were: chronic duodenal ulcus with severe discomforts (29 %), perforated duodenal ulcus (23 %), chronic duodenal ulcus and bulbostenosis (22 %) and bleeding duodenal ulcus (16 %).[4, 5, 7, 10-12]

Preoperative radiological examinations were routinely carried out in all the patients except those operated urgently. The first (early) postoperative follow-up examination was obligatorily performed in all the operated between the eighth and the tenth day following surgery, after the nasogastric probe had been removed, in order to check gastric evacuation.

For patient examination we used 200 ccm of barium suspension of various producers and without a special preparation. Gastrografin was only exceptionally used for check-up for fear of postoperative complications. Late follow-up examinations were carried out from the sixth month following surgery, but only in those patients who came because of some disturbances and suspected relapse.

Checkups covered the subjects from our group of examined patients during the time span of 25 years, i.e. five years after the last operated case.

Based on reports of other authors and our own experience, in radiological treatment of patients we always tried to establish all the direct and indirect signs of peptic ulcus relapse.[1–3, 10] Proved ulcer craters or niches, displayed stenosis with more or less expressed aggravated gastric emptying and repeated morphological findings of suspected lesions during a shorter time period were counted among direct radilogical signs of relapse, whereas more or less aggravated gastric emptying, spastic narrowing of the antrum lumen and plastic pylorobulbar area, mucous membrane oedema of the pylorobulbar area, local sensibility at dosed compression and duodenogastric reflux were among the indirect radiological signs.

However, we always tried to establish the efficiency of pyloroplasty by analysing the appearance of the former area of the pylorus and bulbus. Retained symmetric or asymmetric bulbar base with displayed even slightly dilated pylorus has been regarded as a sign of ineffectual pyloroplasty.[2, 3, 8, 10]

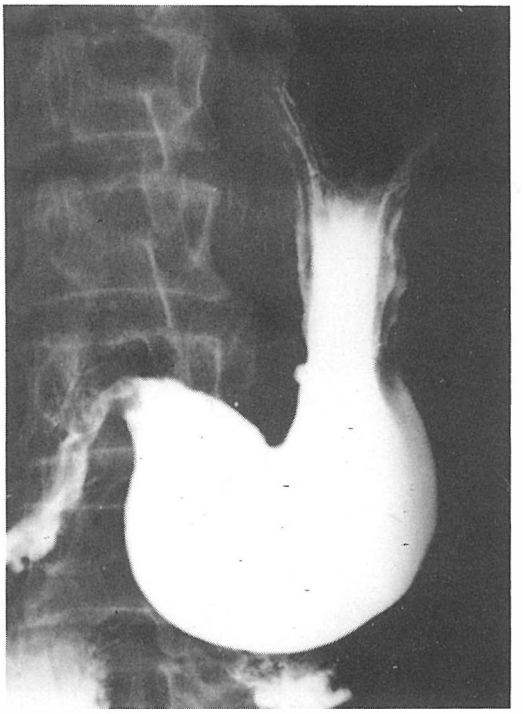

Figure 1a. Relapse of ventricular ulcus without retention.

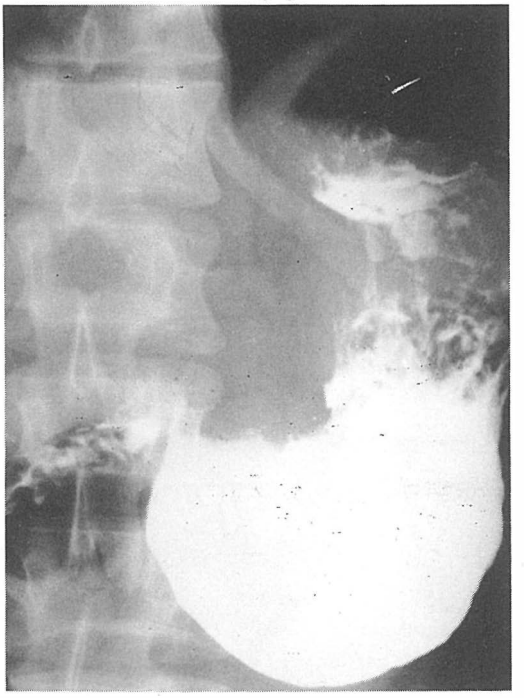

Figure 1b. Retentive ventricular ulcus.

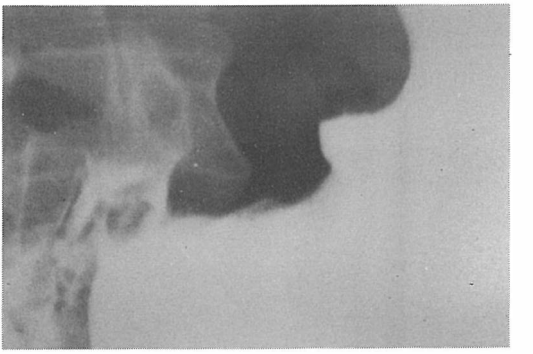

Figure 1c. Penetrating ventricular ulcus.

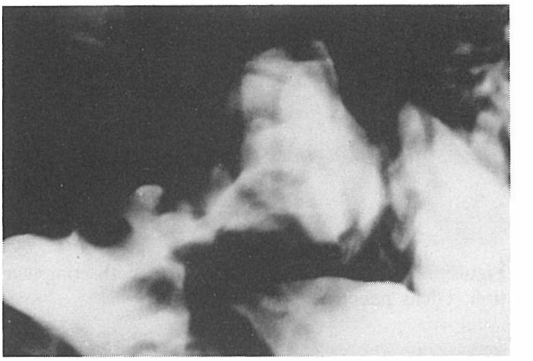

Figure 2a. Relapse of duodenal ulcus shown marginally.

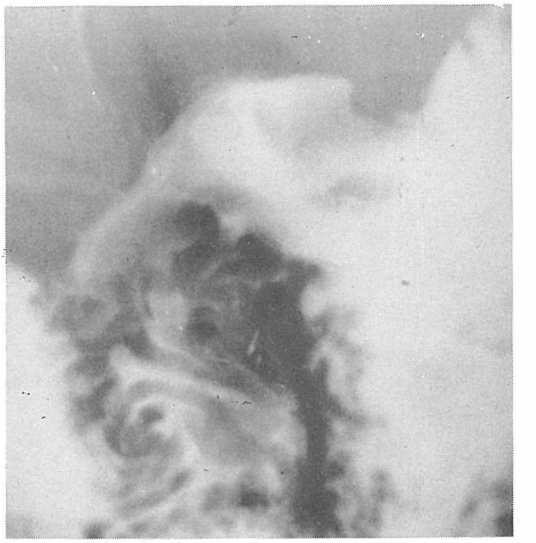

Figure 2b. Relapse of duodenal ulcus and face-on view showing an oval crater.

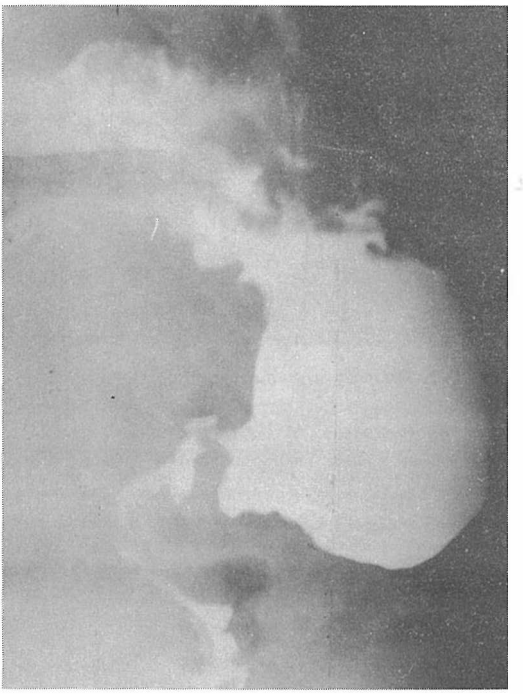

Figure 3a. Relapse of duodenal ulcus with complication. Ulcus penetrans.

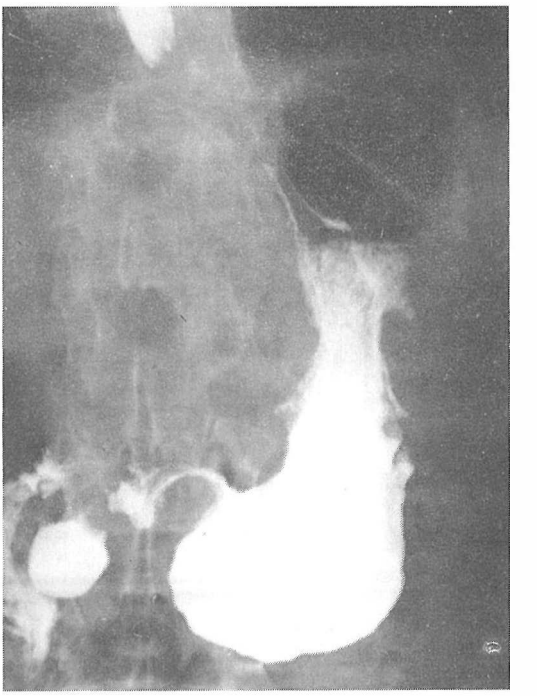

Figure 4a. Stenosis of pyloroplastic area. Narrowing of the oral part with relapse of ventricular ulcus.

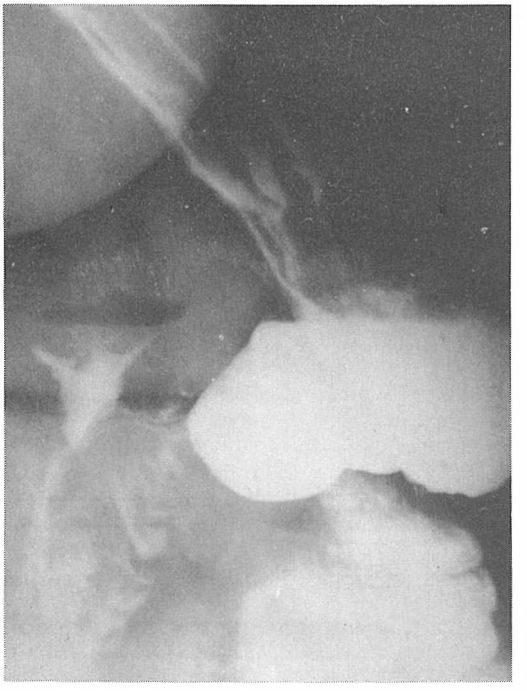

Figure 3b. Relapse of duodenal ulcus with complication. Perforatio tecta.

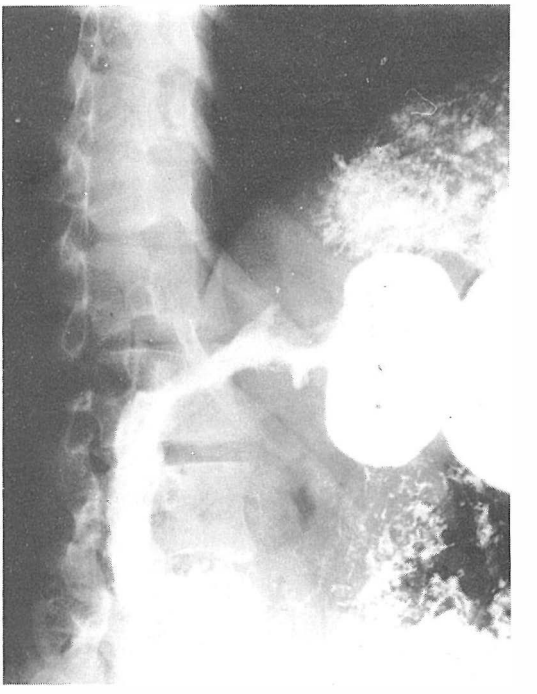

Figure 4b. Narrowing of the whole pyloroplastic area.

Results

Ventricular ulcer relapse has been established twenty-one times, being localized along the lesser curvature (Figure 1a) up to the very border against the duodenum. Ulcer niche finding was accompanied by aggravated gastric emptying in thirteen patients and was conclusive of ulcer retention (Figure 1b). No signs of aggravated evacuation were expressed in eight other patients, whereas typical signs for penetration were observed in three subjects (Figure 1c). We had several retention findings without discomforts and without relapses. In our opinion, it was a question of candidates for relapse.

Pylorobulbar area ulcer relapse has been established eighteen times, but only four patients developed aggravated gastric emptying. Some of indirect radiological symptoms have always been found. Ulcer was more frequently displayed in the form of niche (Figure 2a), and less often as a crater of various form and size (Figure 2b). Relapses were mainly localized at the side of the lesser curvature. Of all the eighteen findings two revealed penetrating ulcers (Figure 3a), while two patients developed perforatio tecta (Figure 3b). All the four findings of complicated duodenal ulcers were characterized by the extension from the side of the lesser curvature towards the area of the lesser omentum. Stenosis of the pylorobulbar area with signs of aggravated evacuation were also established.

Stenosis as a symptom of ulcer relapse without corresponding direct signs of ulceration was found ten times. It has been found as an accompanying symptom in all the patients with complicated ulcer relapse together with signs of aggravated gastric content evacuation. According to the site we found stenosis five times in front of the plastic area (Figure 4a), twice in plastic pylorobulbar area (Figure 4b) and three times aborally from the plastic part (Figure 4c).

Special attention was paid to the time of gastric emptying in the case of indirect signs. The average time value of the initial evacuation amounted to 6 seconds and the complete emptying was 23 minutes within our group of radiologically examined patients. The examined control groups without ulcer showed the average initial evacuation of 33 seconds and the complete emptying time of 1 hour and two minutes under the same conditions.[10] More than one hour till complete emptying, established in our group of the examined subjects, was considered as prolonged.

Based on this criterion, retarded evacuation was recorded twenty-five times; thirteen times with ventricular ulcer relapse; four times with duodenal ulcer relapse and eight times without verified relapse. Of these eight findings a decelerated emptying was observed in five patients in the standing position only. Contrast medium just poured over into the aboral part of duodenum in the right hip lying position. Such finding was recorded only in the case of hook-shaped postoperative stomach with expressed signs of adhesion in the pylorobulbar area. One case developed decelerated evacuation because of spasm and oedema of the antral mucous mem-

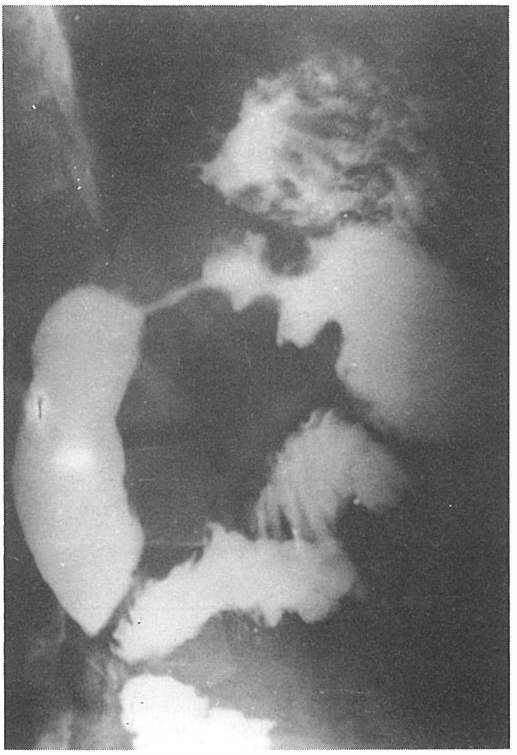

Figure 4c. Strong narrowing of the aboral part.

Table 1. Time of relapse occurrence.

Postoperative years	Number of relapses
0– 1	3
1– 3	38
3– 6	28
6–10	10
10–20	10

brane and the pylorobulbar area. The signs of spasm and oedema withdrew after a drug ulcer therapy and the evacuation time shortened to average values. No organic changes that would be the cause of retarded emptying were recorded in two patients.

Duodenogastric reflux could be presented in the best way in the right anterior lying position when the prepyloric part of the stomach was filled with air. It occurred much more frequently in operated than inoperated patients, but no more frequently in those with proved relapse.

Other indirect signs could be easily radiologically verified, being useful as an additional argument for suspected relapse confirmation.

The time of relapse occurrence has been shown in Table 1 ranging from four months to fifteen years. Most relapses were found in the second and the third year following surgery, with a sudden decrease after the tenth year.

The same group of patients underwent endoscopic examination also, and the parallel findings were numarically presented in Table 2. Endoscopic findings were considered to be closer to a real situation and 7.35 % of relapses, including stenosis, as a real fact.

Discussion and conclusion

Relapse percentage following vagotomy and pyloroplasty cited in literature varies very much, ranging from 2 % to 40 %. The results are not always comparable since they relate to various types of vagotomy and pyloroplasty and different intervals of time after surgery.[2–4,7] For example, Frančišković and co-authors reported 1.8 % of relapses in 1967 and 2.5 % of them in 1972, i. e. 3.5 years following surgery, for our group of examined patients. Šepić (1974) gave the figure of 3.1 % and Dujmović (1985) 3.7 %. We reported the average percentage of 3.9 % 12.5 years following surgery in 1990.[4, 5, 7, 10]

As for the time occurrence, relapses in our group, for the difference from citations of other authors, are represented by a small number during the first year postoperatively. Relapses are mostly found in the second and the third year (45 % approximately). They suddenly decrease after the tenth year, which is in agreement with quotations from literature (Table 1).

Stenosis in pylorobulbar area is a frequent symptom. We consider very expressed stenosis, together with clinical signs, to be a reliable sign of relapse. Therefore, this radiological symptom has been counted among direct signs of peptic ulcus relapse. The site of stenosis, and the extent and length of the narrowed area need to be verified for surgical indication. Sapounov[2, 3] also reports stenosis as a reliable sign of relapse. The standpoint taking stenosis as a secondary consequence of already primarily occurred relapse is only partially acceptable. We

Table 2. Comparative numerical presentation of peptic ulcus relapses verified by endoscopic and radiological method.

	Endoscopic examination				Radiological examination			
	No. of found ulcera	%	of these ulcus penetr.	of these perf. tecta	No. of found ulcera	%	of these ulcus penetr.	of these perf. tecta
Relapse of ventricular ulcer	26	1.91	1	0	21	1.54	2	0
Relapse of duodenal ulcer	54	3.97	0	0	18	1.32	2	2
Stenosis	20	1.47	0	0	12	0.88	0	0
Total	100	7.35	1	0	51	3.74	4	2

believe that a part of stenoses appear independently of relapse occurrence, as a consequence of cicatricial changes in the operated area. So developed stenosis can secondarily generate aggravated gastric evacuation and provide favourable conditions for relapse appearance.

Direct evidence of an ulcer crater or niche of the contrast in morphologically altered pylorobulbar area represents the main problem in the verification of relapse. Plastic technique, formed cicatrices, adhesions and pockets are very likely to produce radiological pictures resembling ulcus craters and niches. An ulcer displayed as a crater represents a special problem. Therefore, most of our relapses are shown as ulcus niches. Changing of their forms during examination indicates that ulcers are out of question. Whether there is a typical fold convergence against the crater or not is of no practical significance because of markedly changed appearance of the pylorobulbar area as a whole, and the fold extension at the site of pyloroplasty. Additional difficulties are caused by fold superposition of the anterior and posterior wall crossing in various directions following pyloroplasty.

Much greater importance should be attributed to the indirect relapse signs than during the examination of inoperated patients. At any rate, all these patients are to be subjected to endoscopic examinations.

The time of gastric evacuation is of special interest. Decelerated emptying is most frequently accompanied by ventricular and duodenal ulcus relapse. Slowed down evacuation was verified in standing position only in one fifth of these patients where relapses have not been found. Gastric content is easily evacuated through usually wide pylorobulbar area in the right hip lying position. These findings are interesting from the relapse-preventing point of view, being most probably a consequence of adhesive changes around the pylorobulbar area and weaker gastric wall tonus. Evacuation control is thought to be indispensable in such cases in lying position also.

Comparison of radiological and endoscopic findings is of great importance for the assessment of peptic ulcus relapse after vagotomy and pyloroplasty. According to our opinion, the preference should be given to the endoscopic examination, especially with ulceration discovered in a deformed pylorobulbar area. This is well evident from Table 2 since the lesser difference of positive findings at verification of ventricular ulcus and stenosis is obvious. A greater number of complicated ulcer relapses associated with radiological examination are worth mentioning here.

Regardless of greater efficacy of relapse detection by endoscopic method,[2, 3, 13, 14] radiological examination is especially important and indispensable for the evaluation of gastric emptying, imaging of the site, extent and length of stenosis and verification of complicated relapsing ulcers. Disregarding the advantage of endoscopic examination, the use of both methods should be supported supplement since they are complementary to each other.

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The radiological symptomatology of congenital duodenal atresia

Ratko Zamberlin, Silvestra Smolčić, Ivo Krolo, Darko Bedek

Clinical Hospital "Sestre Milosrdnice", Zagreb
Radiological and Oncological Institute

Atresia duodeni is a rare disease of the gastrointestinal tract due to disturbed development of the embryo. Over an 8 year period deliveries were observed for the detection of this congenital anomaly in infants in The Obstetrics Department. Out of 12000 infants observed, three were diagnozed at our Institute as having congenital atresia duodeni. Only two cases are presented in this paper. The water soluble iodine contrast medium plus plain film of the abdomen were employed as radiological diagnostic techniques. An accurate and early diagnosis of this anomaly is of a paramount importance since the infant's life depends on timely surgery. The radiological symptomatology, materials, examination methodology and the differential diagnoses are presented in the paper.

Key words: duodenal obstruction-congenital; intestinal atresia-radiography

Introduction

Among congenital malformations of the gastrointestinal tract atresias are the most uncommon ones. Although atresias may occur in any part of the gastrointestinal tract, they extremely rarely occur in the duodenum. When they do, it is mostly in the second portion of the duodenum (pars descendens duodeni) but they can also occur in the third and other portions.[1, 2, 3]

This anomaly is in 60 % of cases associated with other congenital malformations. One third of infants affected by this disease are mongoloids.[4, 5]

Correspondence to: Zamberlin Ratko MD, Radiological and Oncological Institute, Clinical Hospital "Sestre Milosrdnice", Vinogradska 29, 41000 Zagreb, Croatia.

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Materials and methods

Over an 8 year period observation of the deliveries at The Obstetrics Department, 32 out of 12000 born infants were examined because they had symptoms of an obstruction or stenosis in the upper gastrointestinal tract. Twenty infants were males and twelve females.

As radiological diagnostic techniques we employed a plain film of the abdomen and the examination of the upper gastrointestinal tract, using water soluble iodine contrast medium (Gastrografin).

Radiological appearance and discussion

Since this congenital anomaly is incompatible with infant's life, timely radiological diagnosis is extremely important for successful surgery.[1, 6] Possible methods for obtaining an accurate diagnosis are plain films of the abdomen and

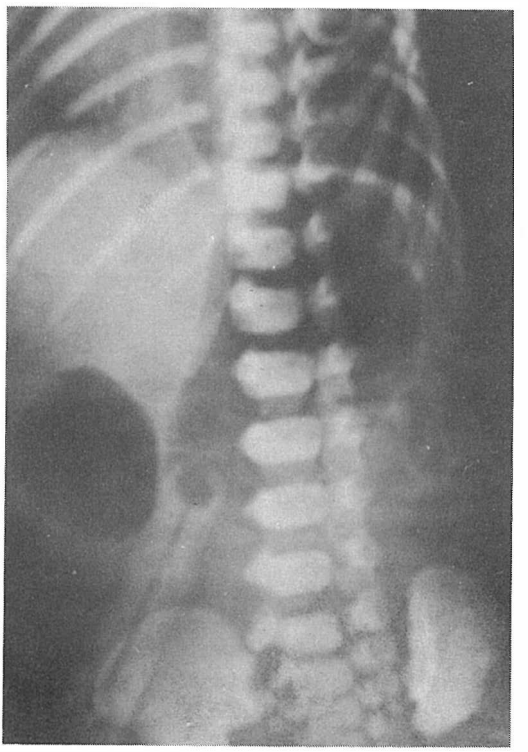

Figure 1a. Atresia of the second segment of the duodenum. Plain film of the abdomen showing "double bubble".

Figure 1b. The same case examined with water soluble iodine contrast medium (Gastrografin).

the water soluble iodine contrast medium examination. If after these examinations it is yet not possible to make a conclusive radiological diagnosis, the examination of the duodenum using water soluble contrast medium along with some drugs (Glukagon, Reglan) i.e. hypotonic duodenography, might be performed.

Sometimes a plain film of the abdomen may be diagnostic. The plain film of the abdomen shows two large air collections, in the upper part of the abdomen "double bubble".[1, 4] One air collection is seen paravertebrally under the left diaphragm and presents the stomach fundus. The other air collection is seen paravertebrally on the right, somewhat lower than the former one and presents the distended portion of the duodenum immediatelly above the obstruction. The lack of air in the lower segments of the small intestine also shows that the obstruction is complete.

Over the period observed we examined 32 infants with symptoms of complete obstruction or stenosis of the upper gastrointestinal tract and found three cases of congenital duodenal atresia. Twenty infants were males and twelve females. The X-ray findings of only two cases are presented. In the first case atresia occurred in the second segment of the duodenum and was associated with mongoloism. The patient was operated on at the Surgery Department in The Children's Hospital Zagreb, but the operation was unsuccessful and the patient died (Figures 1a and 1b). In the second case the obstruction was found in the third segment of the duodenum. The operation performed was successful (Figures 2a and 2b).

In the first case differential diagnosis might consider another congenital duodenal anomaly i.e. pancreas anulare and in the second case radix mesenterii. However, the complete lack

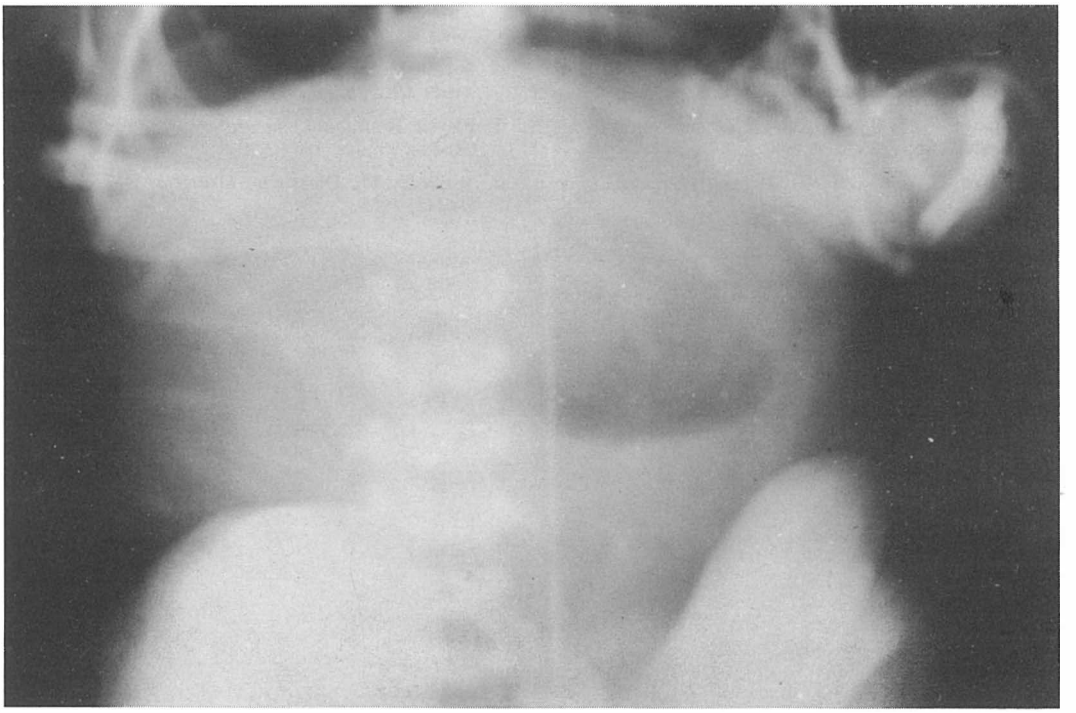

Figure 2a. Atresia of the third segment of the duodenum. Plain film of the abdomen.

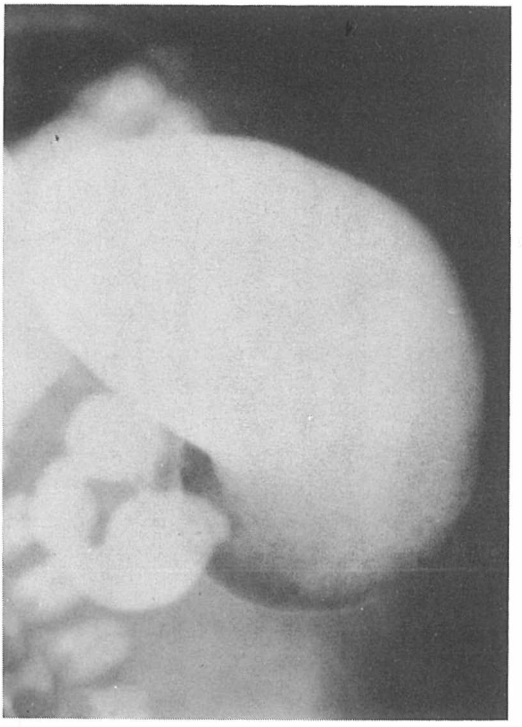

Figure 2b. The same case examined with water soluble iodine contrast medium (Gastrografin).

of air in the lower segments of the small intestine confirms the diagnosis of complete obstruction or duodenal atresia.

The data found in literature suggest that the incidence of this congenital anomaly is 1 in 6000 of infants or 0.017 %.

In the 8 year period from 1984 through 1992, there were three cases of this extremely uncommon anomaly of the gastrointestinal tract identified at our Institute, the incidence ratio being 1 in 4266 or 0.023 %.

Thus, our data show a slightly higher incidence than that reported in literature.

Conclusion

In conclusion, it might be said that the timely radiological diagnosis of this congenital anomaly of the gastrointestinal tract is of a paramount importance for adequate surgical treatment since this is the only efficient way of saving the child's life.

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Algorithm of radiological examinations in the diagnostics of colonic atresia

Marija Frković,[1] Ante Mandić,[1] Ivo Bradić,[2] Božidar Župančić,[2] and Stipe Batinica[2]

Clinical Hospital Center "Rebro"
[1] Department of radiology,
[2] Department of pediatric surgery

Colonic atresia is a rare form of intestinal atresia. During the period 1986–1991, three newborns with atresia of the transverse colon, type III, were diagnosed, and treated surgically. The authors suggest the algorithm of examinations and discuss radiological methods in preoperative treatment of patients and in postoperative course as well as possible complications.

Key words: colon-abnormalities; intestinal atresia-radiology

Introduction

Colonic atresia is a rare congenital anomaly with the incidence of 3–15 % in all intestinal atresias.[1, 2, 3, 4]

It is considered that the occlusion of the mesenteric blood vessels during the 6^{th}–7^{th} week of fetal development is the primary etiological cause of these anomalies.[1, 2, 3, 5, 6]

Colonic atresias can often be found associated with other intestinal[2, 4, 7, 8, 9, 10] and extraintestinal anomalies.[7, 9, 10] They can be located from the cecum to rectum[11, 12, 13] in the form of a diaphragm-type I, as atresia with the fibrous cord between the blind ends without fissura in the mesentery-type II, and in the form of larger or smaller fissura in the mesentery-type III.[1, 3, 14]

Correspondence to: Marija Frković, MD,[1] Clinical Hospital Center "Rebro", Department of Radiology, Kišpatićeva 12, 41000 Zagreb, Croatia.

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Martin and Zerella[9] have classified multiple intestinal atresias as type IV, and Grosfeld[15] has classified multiple "apple peel" small bowel atresias as type IIIb. There are various suggestions about predisposing localizations of certain types of colonic atresias.[11, 12, 13]

Patients with colonic atresia are characterized by clinical and radiological symptoms of low ileus.

Clinical symptoms of the colonic atresia are failure of evacuation of the meconium during the first 24 hours after birth, the abdominal distension and bilious vomiting.

The exact diagnosis of the etiological cause and the level of obstruction is based on radiological analysis. Plain radiograph of the abdomen in supine and upright position is useful for the localization of the level of obstruction.[1, 9] The etiological cause of obstruction can be defined on the basis of barium enema studies.[1, 4, 9, 16, 17] However, with this examination it is not possible to determine either the type of

lesion or the size of the atretic segment. The proximal, preatretic colon is often filled with dense meconium, and in most cases the attempts to define its size using air or perorally given contrast medium remain without result.

Recently, attempts have been made to demonstrate the preatretic segment using ultrasonography (US).[18, 19] These examinations are, in some cases, limited by distended proximal loops of the intestines.

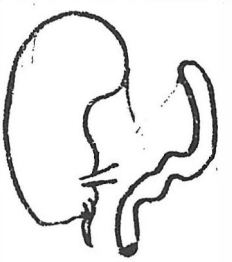
The therapy of this anomaly is surgical. Various surgical treatments performed in two, or more rarely in one stage, from colostomy to direct anastomosis, with or without extensive resection of the dilated preatretic segment of the colon, have been suggested.[2, 5, 7, 15]

Patients and methods

In the last 5 years (1986–1991) we have diagnosed, surgically treated and clinically followed up 3 newborns with congenital atresia of the colon, Type III (Table 1). All 3 infants were born at term, after uncomplicated pregnancies. D. N., a female, and P. N., a male newborn, were transferred from Maternity Hospital to our Surgical department. They were of the same age, and presented with identical symptomatology – absence of meconium, distended, tense abdomen and bilious vomiting. Their general condition allowed adequate preoperative treatment.

US finding showed marked distension of the intestines. Plain radiography of the abdomen in

Table 1. Demonstration of applied diagnostical methods and findings in our patients with colonic atresia.

Name	Sex	Age (hours)	Applied rtg methods	Rtg diagnosis	Surgical diagnosis	Schematic presentation of anomalies
D. N.	f	48	Preoperative – plain radiographs of the abdomen	ileus	colonic atresia type III	
			– US – barium enema	colonic atresia		
			Postoperative – barium enema	normal finding		
P. N.	m	40	Preoperative – plain radiograph of the abdomen	ileus	colonic atresia type III	
			– US – barium enema	colonic atresia		
			Postoperative – barium enema	normal finding		
G. D.	m	96	Preoperative – plain radiograph of the abdomen	pneumoperitoneum	perforation, (p) peritonitis, colonic atresia type III	
			Postoperative I – plain radiograph of the abdomen – US – CT – barium enema	dehiscence, paracolic abscess	dehiscence, paracolic abscess	
			Postoperative II – barium enema	normal finding		

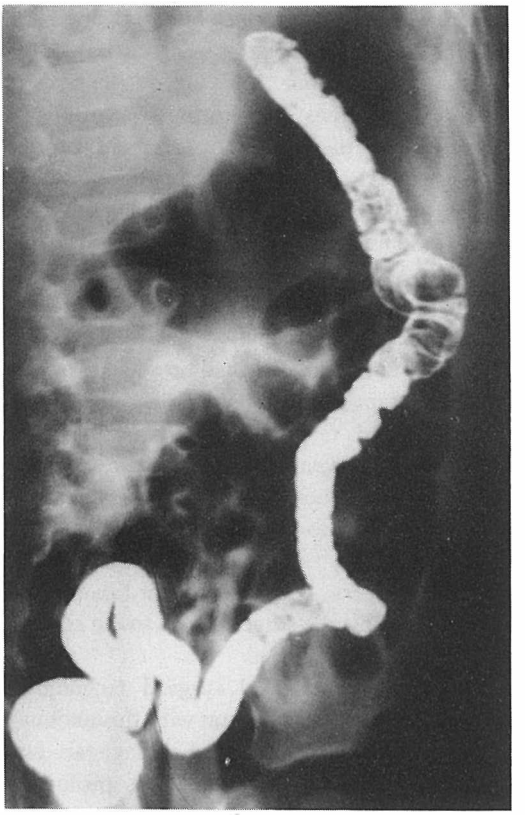


Figure 1. Atresia of the transverse colon. The postatretic segment of the colon with concave-convex proximal contour demonstrated by means of barium enema. The colon is narrow, without meconium.

supine and upright position showed signs of low ileus.

In patient D. N. on barium enema examination, the rectum, sigmoid and the descending colon down to the left flexure were demonstrated (Figure 1). In patient P. N. the colon was demonstrated up to the middle third of the transverse colon. Aboral parts of the colon had narrow lumen, about 1 cm wide, without meconium, with concave-convex proximal ending.

Radiological diagnosis of intestinal atresia was surgically confirmed. In patient D. N. the atretic segment was in aboral, whereas in patient P. N. in proximal half of the transverse colon with wide fissura in the mesentery, type III. The proximal preatretic segment of the colon was dilated and measured 10 cm.

During surgery, the preatretic dilated colon was remodelled by resection of an antimesenteric part in a conically shaped cylinder about 1.5 cm wide at its aboral part. By termino-terminal anastomosis the preatretic and postatretic segment of the colon were connected. The Bauchini valve was preserved. Apendectomy was also performed. Postoperative recovery was without complications.

Third patient, G. D., a male newborn was 4 days old when he was transferred from Maternity Hospital to our Surgical department. On admission he was in a state of prostration, vitally threatened. On native supine and upright radiographs of the abdomen, signs of pneumoperitoneum were found. Surgery was indicated without further radiological examinations. At surgery, atresia of the proximal segment of the transverse colon, type III, was found. The postatretic segment was 1 cm wide. The preatretic segment was approximately 8 cm wide and on its aboral part, about 10 cm from the Bauchini valve, a perforated orifice about 2 cm wide, was seen. In the peritoneal cavity a larger mass of meconium was found.

At first surgical intervention the orifice was closed, the lavage of the abdominal cavity and anus preter on proximal preatretic segment of the colon were done, and antibiotics and parenteral feeding were ordered.

After recovery, during second surgical intervention, remodelling of the proximal preatretic segment of the colon, termino-terminal anastomosis with distal postatretic segment of the colon, and closing of anus preter were done. On the 8th postoperative day complications with sepsis occurred. On plain roentgenograms of the abdomen, in the upper medial abdomen, beside gas in the intestines, aeroliquid levels which were identified to be paracolic abscesses, were seen. There were no signs of ileus. US and CT have not confirmed the diagnosis of abscess. Barium enema was indicated. Using barium water mixture, aboral part of the colon was demonstrated. Close to the anastomosis, the lumen of the colon was reduced to a narrow track of contrast medium which filled the irregular cavity of paracolic abscess towards the

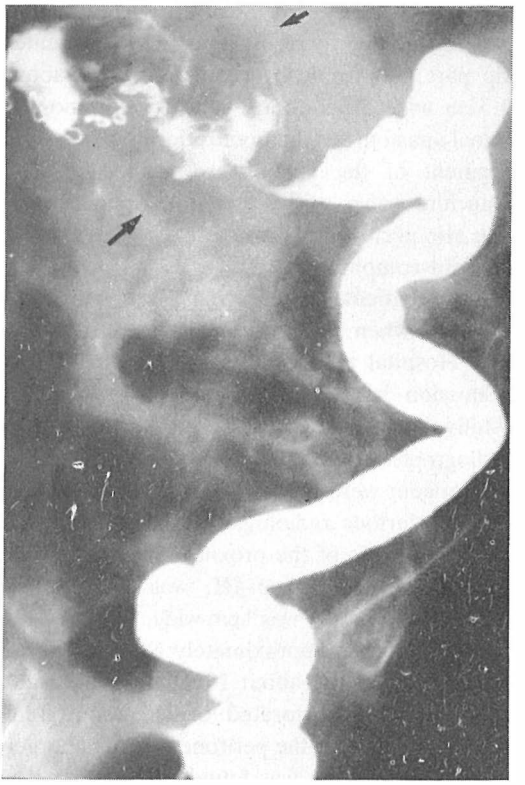


Figure 2. Postoperative complication, dehiscence of termino-terminal anastomosis and paracolic abscess (→).

caudal contour of partly dehiscented suture (Figure 2).

The child was reoperated. The postoperative course with intensive antibiotic therapy was without complications.

Discussion

The aim of our study was to assess the possibilities and limitations of radiological methods because prognosis of the patients with colonic atresia depends on correct and early diagnosis.

The diagnosis of low ileus was established on the basis of plain abdominal roentgenograms, and the etiological cause of ileus was found using barium enema examination. "Hook sign",[16] "cul-de-sac",[12] or concave-convex proximal contours of postatretic segment of the colon demonstrated by use of contrast medium, are important signs in the diagnostics of this pathologic condition. However, on the basis of these examinations, neither the type of atresia nor the size of the atretic segment can be diagnosed. At surgery, in all 3 patients, atresia of the transverse colon, type III, was found. It is the usual predisposing site of this type of atresia.[11,12]

The possibilities of US and CT in the preoperative diagnostics are limited by large quantities of gas present in the proximal bowel loops.[18,19]

The therapy of these anomalies is surgical. Its aim is to restore the continuity of the intestines. The type of the surgical intervention depends on the location of atresias, their number, associated anomalies and physical status of patient.[3,4,5,7,9,12] Our two patients underwent only one surgery, whereas the third patient G. D. underwent three surgeries due to the complications described above.

Despite the advanced surgical techniques, the mortality rate of children with this anomaly is very high, especially if the diagnosis and indication for surgical treatment is prolonged which can cause the perforation of the intestines.[6,9,10,20,21,22]

The possibility of development of functional obstruction in the postoperative treatment after restoration of intestinal continuity, which can also lead to lethal outcome, is discussed in literature.[23]

In our opinion, in our patient G. D. the association of all previously mentioned parameters has contributed to the complicated course of illness, but fortunately, without lethal outcome.

On the basis of plain roentgenograms and barium enema studies the status of colon, anastomosis, postatretic segment of the colon after surgery, as well as possible complications can be diagnosed. US and CT examination in this period of illness are inadequate.

In summary, on the basis of our own and other authors' experience, we suggest the following algorithm of examinations in the cases suspective of colonic atresia:

1. US is a method of limited possibilities in the diagnostics of this pathology. We recommend it as a screening method in less complicated cases.

2. Plain roentgenograms of the abdomen in supine and upright position are useful in the diagnostics of the level of the obstruction.

3. Barium enema is a necessary diagnostic method in defining the level and the etiological cause of the obstruction.

4. Barium meal examination or any other radiological method (CT) with regard to its harmfulness and usefulness is not justified in the diagnostics of this pathology.

The postoperative follow-up of the morphological and functional status of the colon requires barium enema examination. Due to the possible preoperative or postoperative complications, the clinical status of a patient can modify the algorithm of examinations.

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Resolving of mammographically visible though clinically undetectable lesions suspicious for breast cancer

Jurij Us

Institute of Oncology, Department of Diagnostic Radiology, Ljubljana, Slovenia

The results of active screening for breast cancer are presented. The study included 60 women with mammographically detected breast lesions which were clinically not palpable, though their mammographical findings were suspicious for breast cancer. In all 60 women, localization of the breast lesion was performed by means of a wire according to the Franken's method. Breast cancer was established in 16 patients (26.6 %), 7 of which (43.7 %) had non-invasive and 9 (56.3 %) invasive cancer, whereas benign dysplasia was found in 44 women (73.4 %).

Key words: breast neoplasms-diagnosis; mammography

Introduction

Nowadays, breast cancer detection is based on two essential diagnostic methods: 1) clinical examination (CE) and X-ray imaging of the breast, i.e. mammography (MG). The findings of both examinations require additional microscopic verification. Clinically detectable (palpable) breast lesions can be best explained by fine needle aspiration biopsy (FNB). According to the recommendations of the European Breast Cancer Study Group (EBCSG), active screening for early breast cancer should be carried out in women without symptoms of breast cancer. Thus, asymptomatic women over 50 years of age should be subjected to regular mammographic examinations in 2–3 year intervals. Such an approach is expected to contribute to a significant decrease in breast cancer mortality.[1] Regardless the fact that mammography is a method that can detect breast cancer at a stage when it is not assessable by any other available method, the diagnosis is regarded incomplete without a clinical examination. Up to 63 % rate of false negative mammographic findings in women under 35 years of age reported in the literature can be attributed to the density of parenchyma in young women, whereas in women over 35 years of age mammography fails to discover up to 15 % of clinically detectable tumors.[2]

Mammographically detected changes suspicious for breast cancer require further explanation. According to the recommendations of EBCSG, such changes should be marked by radiologist to facilitate their exact positioning at surgery. Surgically removed part of the breast is then again X-rayed in order to make sure that the suspicious tissue has been actually removed; at the same time the lesion is marked

Correspondence: Prim. Jurij Us, MD, Department of Diagnostic Radiology, Institute of Oncology, Zaloška 2, 61105 Ljubljana, Slovenia.

UDC: 618.19-006.6-073.75

for better and more effective histopathologic examination.[3, 4, 5]

The lesion can be easily marked by means of a thin stainless-steel wire with a hooked tip.[6] In this way both the change and the mark can be easily imaged on mammography, thus facilitating the interpretation of mammographical finding and positioning of the lesion on surgery.

The surgeon orientates the removed breast tissue by marking its front and upper edge and sends it to the radiologist for X-ray examination (Figure). During the procedure the tissue sample is placed on a Petri dish filled with paraffin. The dish with the specimen is placed into a special device which enables marking of the suspicious lesion for fast and accurate histologic examination.[7]

Material and methods

In the years 1986 to 1992, changes suspicious for breast cancer were localized in 60 women in the age of 36–69 years. Mammographically suspicious though clinically undetectable changes were as follows: asymmetrical breast structure, accentuated tissue density, the presence of stellate formations, a cluster of 5 or more microcalcinations appearing alone or associated with the above mentioned changes, and finally, a mammographically evident tumor.

The size of localized changes ranged from a hardly perceptible cluster of microcalcinations to a tumor with the diameter of 2 cm.

In the case of a mammographically detected suspicious breast lesion, further diagnostic and therapeutic procedures were agreed upon by both the surgeon and the radiologist. Surgery was performed either on outpatient basis, when no major intervention had been expected, or the patient was admitted to the ward a day before surgery taking into account possible need for radical surgery.

Mammography was repeated again prior to surgery and premedication. Approximate positioning of the lesion was done by means of a special localization plate. The inserted wire was fixed with a piece of adhesive tape and the puncture site protected with sterile gauze. The patient was operated on within two hours after the localization procedure.

The breast tissue severed on surgery was X-rayed by means of a special device equipped with coordination system which helped us to find the removed lesion; the surgeon was immediately informed about the outcome of the procedure. For the needs of radiologic investigation the removed breast tissue was placed on a Petri dish filled with paraffin which enabled localization of the lesion by means of injection needles. Thus prepared specimen was again X-rayed. The method has been named "sample mammography" (SM). During sample taking procedure, the radiologist assisted the pathologist by explaining the SM image in order to enable him to determine the most suitable site for sample taking.

Case 1:

Patient M.V., born 1952, patient record no. 3105/82, has been referred to our Institute because of the enlarged right axillary lymph nodes. FNAB revealed the presence of light-cell carcinoma. The site of primary tumor could not be found. The patient underwent mammography, though the obtained mammograph showed only a dense homogeneous shadow which was diagnostically irrelevant owing to the patient's breast type (Wolfe DY). On the other hand, this type of the breast, which is known to be rather unyielding to mammography, is associated with the highest incidence of breast cancer. As the radiologist found a suspicious density in the lower inner quadrant of the breast, a blind biopsy of that site was performed. On pathological examination no evidence of malignoma could be found in the surgical specimen. Taking into account the possibility that formerly diagnosed light-cell carcinoma could originate from the kidney, intravenous urography was performed as well; the findings, however, were within normal limits. The radiologist who carried out the procedure reviewed previous radiograms, and discovered a cluster of microcalcinations suspicious for breast cancer in the outer upper quadrant of the right breast. After consultation

with surgeon, he carried out localization of the microcalcinations. Postoperative sample mammography confirmed that the changes had been removed. Pathomorphological examination of the removed breast tissue revealed the presence of an infiltrative ductal light-cell carcinoma; it was moderately differentiated, with strongly expressed fibrous stroma. The tumor was of the same structure as previously discovered lymph node metastases. Subsequently, the patient underwent radical mastectomy.

Case 2:

Patient N.M., born 1923, pat. record no. 2643/86, was asymptomatic. She decided to undergo breast examination because her niece, a medical nurse, advised her so.

She had always been healthy. She got menarche at the age of 14 and had been postmenopausal for 15 years already. She gave birth twice and had one abortion.

Clinical examination showed evidence of normal involutive breast. On mammography a small stellate formation suspicious for breast cancer was imaged in the outer upper quadrant of the left breast.

Localization was done by means of a wire (Figures 1 and 2). The removed part of the breast was X-rayed (Figure 3) again, and the suspicious lesion in the sample marked. Pathomorphological diagnosis was intraductal infiltrative carcinoma of the breast, 7 mm of size; this finding corresponded to the so-called "minimal breast cancer" which is considered curable.

Results

We have performed 60 localizations of suspicious breast lesions. Of these 16 (26.6%) turned out to be breast cancer, whereas benign displasias were found in 44 cases (73.4%) (Table 1).

There were 7 (43.7%) noninvasive and 9 (56.3%) invasive breast cancers (Table 2).

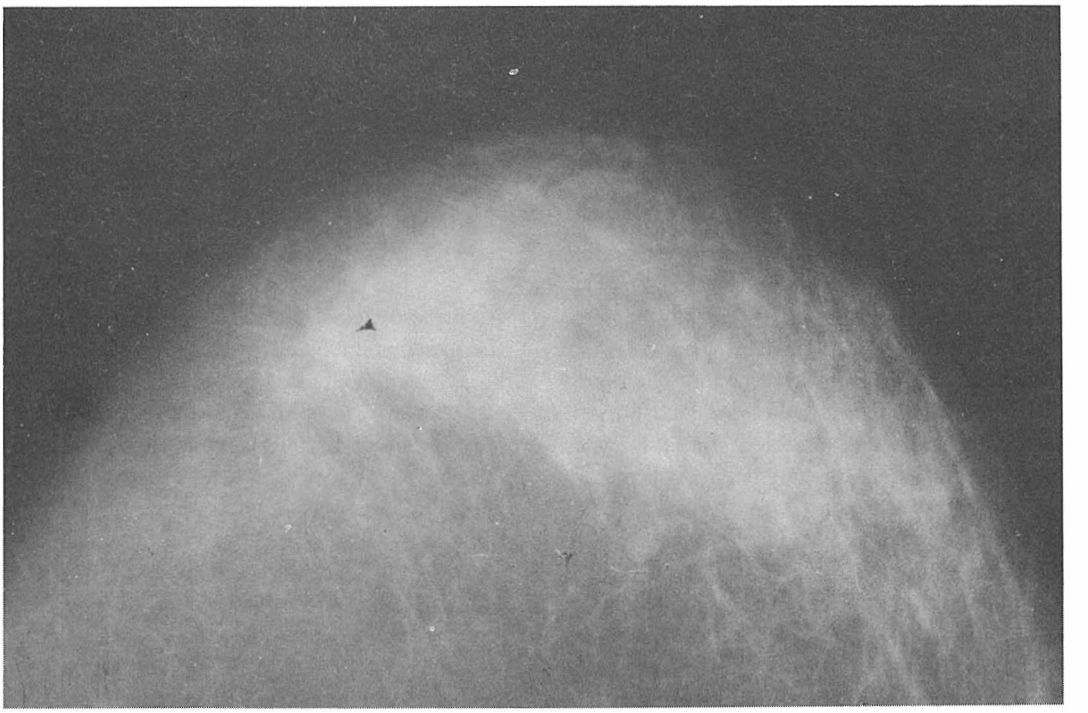

Figure 1. Craniocaudal plane. Wire hook is in the immediate vicinity of the lesion.

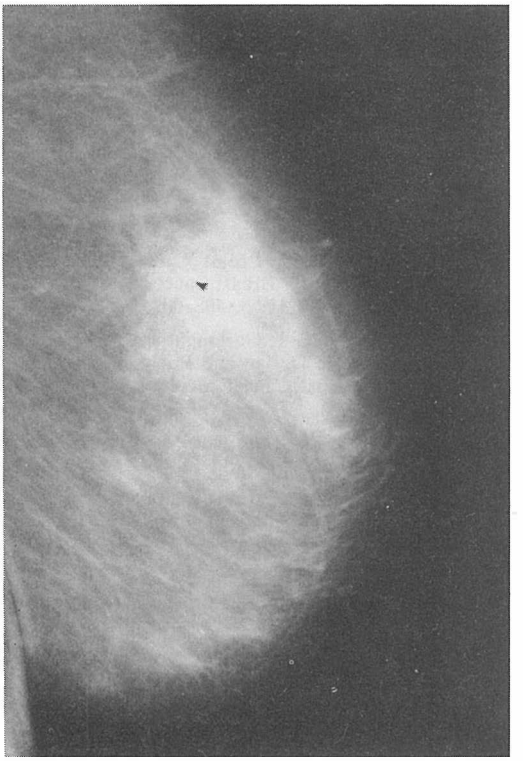

Figure 2. Mediolateral plane. Wire hook is in the immediate vicinity of the lesion.

Noninvazive lobular breast cancer was found in 2 women, and initial ductal carcinoma in 5. Of invazive breast cancers, 4 originated from the ducts, whereas another 4 were lobular and one was of mixed type (lobular and ductal).

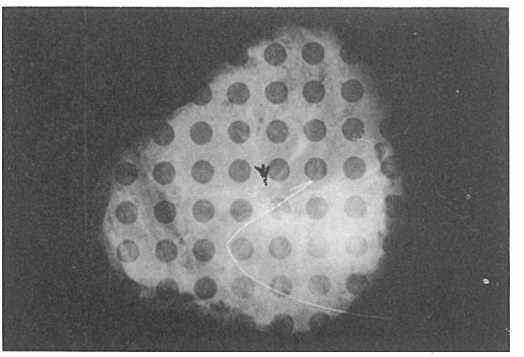

Figure 3. Sample mammography. A stellate formation can be seen in the removed tissue sample. Holes in the device enable precise positioning of the site for bioptic sample taking. (See Case 2. Intraductal infiltrative breast cancer, 7 mm of size.)

Table 1. Suspicious breast lesions.

Surgically treated patients n = 60 (100 %)	
Diagnosed	
breast cancers n = 16 (22.6 %)	benign dysplasias n = 44 (73.4 %)

Table 2. Established breast cancers.

Diagnosed breast cancers n = 16 (100 %)	
Noninvazive n = 7 (43.7 %)	Invazive n = 9 (56.3 %)

Discussion

Localization of changes in the breast is a simple, fast and reliable method which helps to resolve mammographically evident lesions suspicious for breast cancer. The diagnosis of cancer was confirmed in more than one fourth of our patients. According to the reports from literature, about 20–40 % of cancers in surgically treated patients are discovered by the help of this method. The rate of established cancers vs benign displasias depends on the criteria used by the radiologist when assessing a change as suspicious for breast cancer. Undoubtedly, with respect to a high rate of established breast cancers these criteria must be very strict. A question remains, however, how many initial (noninvazive) breast cancers failed to be detected owing to a too restrictive approach. In our report, almost a half of the established cancers were noninvazive (7/16). This undoubtedly proves that our selection criterium was relatively good.

Self-evidently, initial cancer, particularly when situated deep in the breast, is not accessible to clinical examination. It seems also justified to question why tumors as large as 2 cm

need to be localized. But everyone who is involved in the diagnostics of breast diseases should be aware of the fact that every now and then enormously large breast can be seen. When, apart from their size, such breasts are also clinically difficult to assess, it seems quite logical that – though exceptionally – even a relatively large tumor can be easily overlooked on clinical examination.

Conclusion

Mammography of the breast still remains the method of choice for the detection of very small changes that cannot be evidenced by clinical examination. Both mammographical and clinical findings must be microscopically confirmed in order to serve as a basis for treatment selection.

Localization of mammographically evident changes suspicious for breast cancer is a fast, simple and reliable method which facilitates the surgeon to determine the correct site for sample taking. Surgically removed tissue should be again radiographically examined so that the site of bioptic sample taking can be determined.

All these findings have been confirmed by the results of our study.

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Computerized tomography of the orbit

Martin Čerk

Institute of Diagnostic and Interventional Radiology, University Medical Center, Ljubljana, Slovenia

The role of computerized tomography in the diagnosis of orbital diseases is presented. The problems of radiation and protection are particularly pointed out as it is believed that the investigation-related radiation dose may be high enough to produce a cataract.

Key words: orbital diseases; tomography, x-ray computed

Introduction

Computerized tomography (CT) is a computer-quided X-ray imaging method. Owing to its good resolution, thin sections and short exposure time CT is suitable for imaging of the orbit as well as of other formations of the skull base.

The bony structure of the orbit and its contents is examined using axial and coronal (transverse) planes.[1] An image in other plane can be reconstructed by means of a computer in the same way as e.g. an image in the sagittal or frontal plane can be reconstructed from axial sections. Apart from the fact that the resolution of such images is generally of a lower quality, also the measurements of absorption values are not sufficiently accurate. Besides, absorption measurements on a CT with poor resolution are also of inferior quality. A better reconstruction of images can be obtained by partly overlapping sections, however, this approach requires a greater number of sections to be done, which results in a higher exposure of the patient to radiation. In order to calculate the volume of e.g. fatty tissue in the orbit a number of sequential parallel sections is needed. Adverse effects of x-rays are particularly evident on the eye lens where they may give rise to a cataract. Critical absorption doses able to cause this condition range between 2-15 Gy (Gray),[2] depending on the age of the patient (1 Gy is a unit used in dosimetry, denoting absorbed energy per mass unit of matter, i. e. 1J/kg; 1 Gy = 100 rad).

Correspondence to: Martin Čerk, MD, Institute of Diagnostic and Interventional Radiology, University Medical Center Ljubljana, Zaloška 7, 61000 Ljubljana, Slovenia.

UDC: 617.76-073.756.8

Radiation dose per eye lens

Radiation dose to the eye lens received by the patient on CT of the orbit is in direct correlation with

- number of sections,
- thickness of sections
- mAs product
- direction of sections with respect to the eye lens (Figures 1, 2, 3, 4, 5).

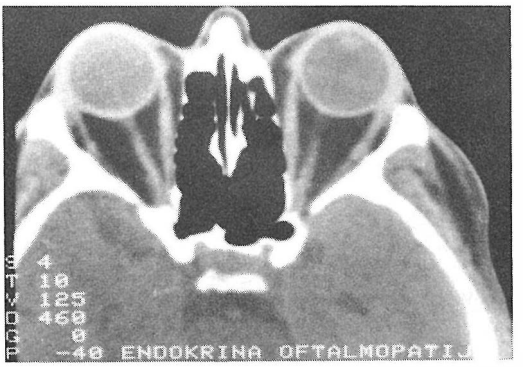

Figure 1. Small exophthalmus and enlargement of the extraocular muscles and orbital fat as well (magnification).

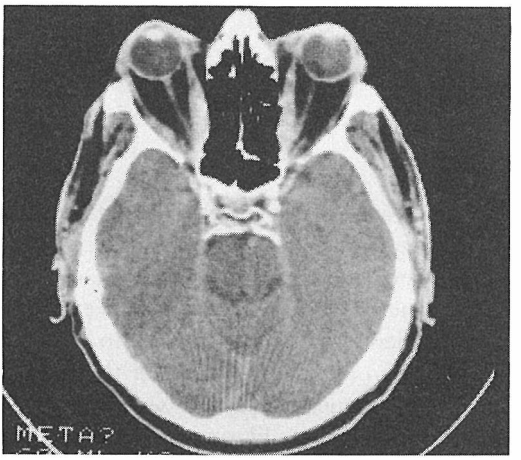

Figure 2. Large exophthalmus and huge enlargement of orbital fat, and increase in the size of medial muscles.

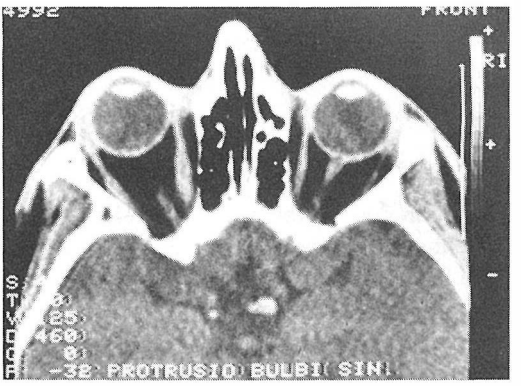

Figure 3. Exophthalmus of the left eye and enlargement of the medial extraocular muscle.

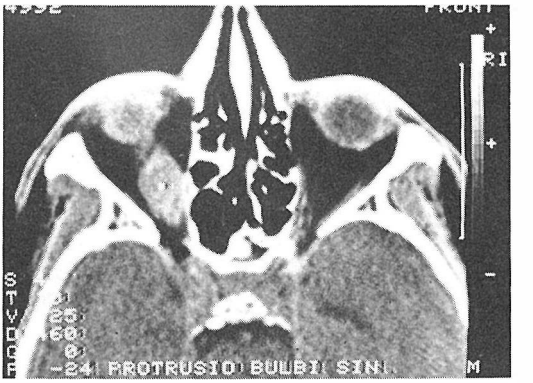

Figure 4. Retrobulbar tumor of the left orbit.

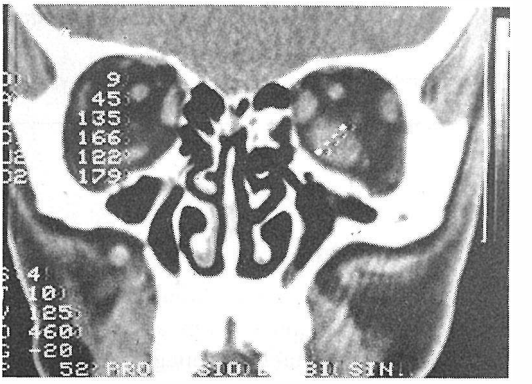

Figure 5. Retrobulbar tumor between medial and inferior extraocular muscles. Both muscles are changed (coronal projection with magnification).

The highest radiation dose to the eye lens is received when the eyeball is in the direct beam of X-rays. Total dose received in an examination of the orbit using a sequence of closely parallel thin axial sections is 20 mGy, whereas the dose with coronary sections amounts to 47 mGy. In the section thickness of 2 mm we use 780 mAs product, in 4 mm 460, and in 8 mm 230. Thus the total dose to the eye lens received during examination of the orbit using 4 mm sections is only 20 mGy, whereas with 2 mm sections the dose amounts to 52 mGy. Thin sections provide a more accurate information and a better image owing to the elimination of data pertinent to the adjoining structures,

though in this case a much higher number of sections is needed for imaging of the same structure.[3]

Conclusion

In CT examination of the orbit as low a number of maximum thin target sections as possible should be made by means of a machine that can produce a good-resolution image in a very short exposure time. Nevertheless, magnetic resonance should be used preferably for examination of the orbit, whenever available. In this way the risk of a cataract and associated with that further damage of the eye, which has already been affected by different conditions such as e.g. endocrine ophthalmology, can be significantly reduced.

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Evaluation of metastatic invasion in the wall of main neck vessels. Conventional versus color-coded ultrasonography

Mirna Juretić,[1] Alan Šustić,[2] Željko Fučkar,[2] Marijan Car[1]

[1] *Department of Maxillo-facial Surgery*
[2] *Ultrasound Unit, University Hospital, Rijeka, Croatia*

Conventional ultrasonography and color-coded sonography are used in evaluation of the relationship between metastatic tumor vs the wall of large blood vessels of the neck, i. e. the common carotid artery and its main branches, as well as the internal jugular vein in 34 patients with malignant tumors of the maxillo-facial region. The results have not shown any significant difference between the two sonographic methods, as both proved to be highly sensitive (100 %) and specific (84-86 %).

Key words: carotid artery diseases-ultrasonography; jugular veins-ultrasonography; neoplasm metastasis;

Introduction

Malignant tumors of the oral cavity and maxillo-facial region metastasize mainly into the lymph nodes of the neck. Modern diagnostics, beside clinical examination includes also »blind« or sonographically guided aspiration biopsy, computerized tomography of magnetic resonance.[1, 2, 3, 4, 5, 6] Ultrasonography has developed rapidly in the last few years due to swift progress of medical technology. The construction of high-resolution high-frequency transducers has enabled visualization of very tiny formations, and by the introduction of duplex sonography, especially color-coded flow mapping (CD-sonography) into clinical practice, and excellent presentation of vascular body-system was achieved.[4]

From surgical point of view, one of the basic preoperative information is the relation of metastatic process to the large blood-vessels, namely the common carotid artery and its main branches, as well as v. jugularis interna.

As evident from recent literature, CD sonography is an non-invasive method which enables excellent presentation of blood vessels and hemodynamic conditions, and therefore we have decided to correlate this method with conventional sonography of the neck. Using our own casuistics, we have tried to assess metastatic invasion toward main vessels of the neck by means of both methods, and later on, intraoperatively confirm the obtained findings.

Correspondence to: Marjan Car, MD, Ph.D., Department of Maxillo-facial Surgery, University Hospital Rijeka, Krešimirova 42, 51000 Rijeka, Croatia.

UDC: 616.133-033.21:616.145.2-033.2:534-8

Patients and methods

In the period from September 1, 1991 to September 1, 1992, 34 patients with malignant

tumors of the maxillo-facial region and metastatic involvement of the neck lymph nodes were treated at the Department of Maxillofacial Surgery (University Hospital Rijeka, Croatia). The age of the patients ranged between 35-81 whereas the male – female ratio was 82-18 % in favor of male patients, respectively.

Conventional sonographic examination was performed on the ultrasound apparatus Aloka SSD LS 280 with a linear transducer of 5 MHz, whereas for CD sonography a color-coded apparatus Hitachi EUB 515 with a convex transducer of 5 MHz was used.

The findings were considered negative when the blood-vessel walls were intact, and positive when they were invaded by secondary tumor. All cases were examined by two independent, equally qualified specialists. Hemodynamic parameters obtained by Doppler analysis are not presented. The malignant nature of secondary deposits was verified preoperatively by sonographically guided fine-needle aspiration biopsy, and later on by postoperative pathohistological analysis.

Results

Previously verified metastatic deposits of the neck have been visualized by preoperative conventional ultrasonography and CD sonography. All findings were later on intraoperatively evaluated and the results tabulated (Table 1).

Correlating conventional vs CD sonography, a minimal statistically insignificant difference has been observed. The sensitivity of both methods is 100 %, whereas specificity for CD technique and conventional sonography is 84 % and 86 % respectively. Positive predictive value ranges between 60 % (conventional ultrasonography) and 50 % (CD), whereas negative predictive value for both methods is 100 % (Table 2).

Table 1. The relation of metastatic tumor versus a. carotis (comm., int., ext.).

	Conventional US	CD sonography	Interventional finding
Negative	29/85 %	28/82 %	31/91 %
Positive	5/15 %	6/18 %	3/9 %
Total	34/100 %	34/100 %	34/100 %

Table 2. The ralation of metastatic tumor versus v. jugularis int.

	Conventional US	CD sonography	Interventional finding
Negative	21/62 %	21/62 %	25/74 %
Positive	13/38 %	13/38 %	9/26 %
Total	34/100 %	34/100 %	34/100 %

The results in the group, where the relation between metastatic tumor vs vena jugularis interna was evaluated, have been identical in both sonographic methods: sensitivity 100 %, specificity 86 %, positive predictive value 69 % and negative predictive value 100 % respectively (Figure 1, 2).

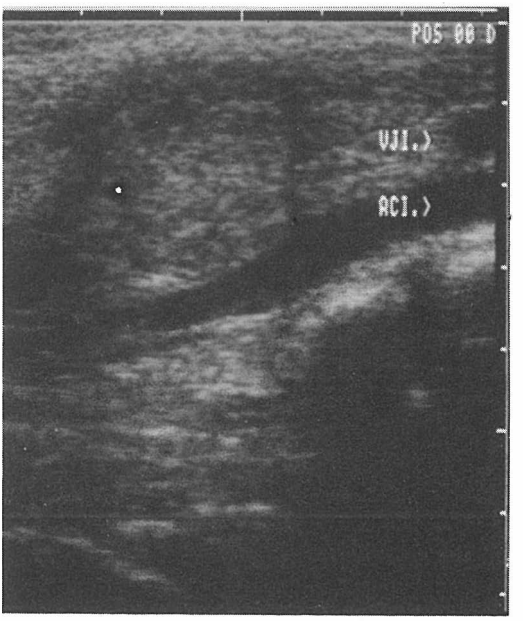

Figure 1. Destruction of the internal jugular vein (VJI) and compression of the internal carotid artery (ACI) with metastatic deposit. The arterial wall is intact (conventional sonography, 5 MHz).

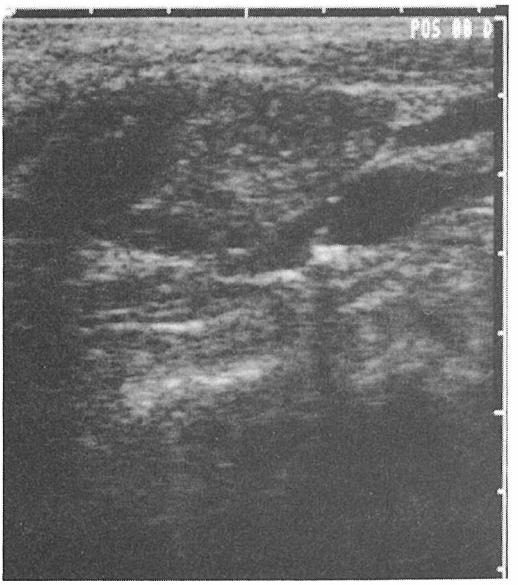

Figure 2. Destruction of both the internal jugular vein and common carotid artery (conventional sonography, 5 MHz).

With reference to the presented results it is important to emphasize that the hemodynamic parameters obtained by Doppler analysis (PI, RI, etc.) have not been presented owing to the fact that pathoanatomical substratum of vessel--wall lesion is not in direct correlation with the degree of hemodynamic perturbations in early stages of the disease. Compression of the vessel lumen certainly alters numerical results obtained by quick Furier's transformation, however, summing up personal experience and data from relevant literature, no direct correlation between the damage of blood-vessel wall and hemodynamical disorders has been established.

Discussion

Color-coded sonography is a new non-invazive method which has in many ways improved conventional sonographic diagnostics. The present prospective study has been undertaken in the belief that this method may also increase preoperative evaluation of blood-vessel wall lesions caused by metastatic processes. However, the results have not shown any significant difference between the two sonographic methods. Both were found to be highly sensitive, and their specificity was quite adequate (between 84-66%). Low positive predictive value (50%, 60%, 69%) should be attributed to a relatively small group of patients.

Conclusion

Conventional sonography is the method of choice in evaluating metastatic invasion of the blood-vessel wall of neck tumors.[1,2,3,4] Its advantages such as low cost, rapidity of investigation, no risk of exposure to irradiation and high diagnostic value have been often mentioned in the relevant literature.[2,4] In many aspects, the more expensive color-coded sonography represents a certain improvement of the standard ultrasonic diagnostics, but nevertheless, the present study has not been able to demonstrate it.

Conventional ultrasonography still remains the best method for the evaluation of metastatic tumors vs vascular body of the neck. Of course, CD-sonography is recommended for the assesment of hemodynamic disorders caused by blood-vessel compression, and also as an adjuvant procedure to the routine neck examination in cases of primary malignant tumors of the maxillo-facial region.

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Colonic sonography

Nikola Ivaniš, Milivoj Rubinić, Relja Perić, Duško Banić, I. Kraus

Clinical Hospital Centre Rijeka
Clinic of Internal Medicine and Institute of Radiology

The authors' experience in sonography of the colon filled with water is described. This is a relatively new method reported in medical literature of the recent five years. Our experience so far confirms the great value of this method in the diagnostics of tumours and polyps, as well as of inflammatory diseases (ulcerative colitis and Crohn's Disease) of the colon. Compared with colonoscopy, its results are particularly valuable. Out of the 53 colonosonographies there were only three false positive findings, as compared with colonoscopy, which confirms the reliability of the former method. The very good results of this method are apparent in the evaluation of the spread of colonic cancer to adjacent structures.

Key words: colonic diseases-ultrasonography

Introduction

The importance of conventional sonography in the diagnostics of colonic diseases is not negligible, but is nevertheless limited by the length of this organ and the fact that it is filled with bowel contents. Hence, there are few reports on the use of sonography in the diagnostics, especially of colonic cancer.[1, 2, 3]

Well-known are also the possibilities of endoscopic sonography, in this case particularly transrectal, the possibilities of which in the diagnostics and evaluation of the spread of rectal cancer are incontestable and quoted by a great number of authors.[4–7]

Correspondence to: Nikola Ivaniš MD, Clinical Hospital Centre Rijeka, Clinic of Internal Medicine, B. Kidriča 42, 51000 Rijeka, Croatia.

UDC: 616.348-073:534-8

The method presented here is relatively new and has a great practical value in the diagnostics and follow up of the extent and treatment results of bowel diseases. It is equally valuable in case of tumorous as well as inflammatory diseases of the colon.[8–13]

Material and methods

The ultrasound examination of the colon has been adopted by our institution as well as by a great number of other centres practically as an everyday routine procedure. The non-invasive character of this method renders it one of the most frequently used techniques in contemporary diagnostics. But in addition to this method, some more invasive methods are also used routinely, of which the endoscopic ones come first and foremost.[14]

An essential requirement in colonic sonography is as thorough as possible purging of the

patient's bowels. For better relaxation of the colon one of the spasmolytics is administered. By means of a catheter inserted into the rectum the colon is filled with 1500 to 1800 ml of water. The ultrasound examination of the colon is started as soon as water begins to be instilled. It is carried out by means of an ultrasound apparatus and Convex probe of 5 MHz. The average duration of the examination ranges from 25 to 30 minutes.

So far 53 colosonographic examinations have been carried out in our institution during a one-year period.

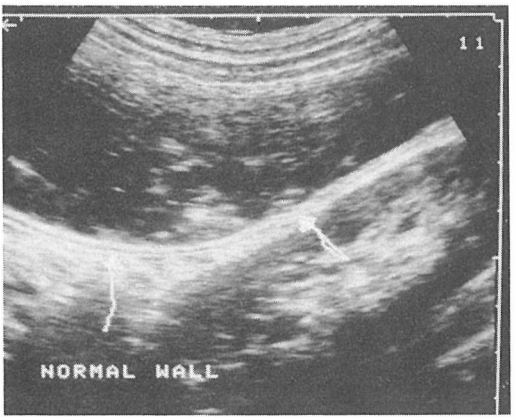

Figure 1. Normal colon wall.

Results

In nine cases the findings were normal, whereas in 28 patients colonic carcinoma was found; eight patients had polyps of the colon, five of them with typical signs of Crohn's Disease, and three of ulcerative colitis. With all of them this method was easy to perform and practically painless. In all these cases the results were verified by colonoscopy, and in the case of patients with colonic carcinoma the diagnosis was confirmed also by surgery.

In our group of 53 patients there were three false positive findings. The first was the case of the remains of the content in the cecum misinterpreted for a polyp, which was rulled out by colonoscopy. The second case was wrongly diagnosed as a polyp of Valvula Bauchinis; in reality it was the prolapse of the same, confirmed by total colonoscopy, the third case was first explained as a stenosis of the colon, and later on confirmed by surgery as an adhesion.

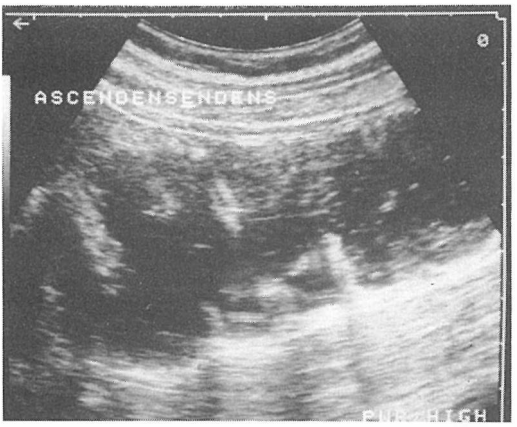

Figure 2. Normal colon haustration.

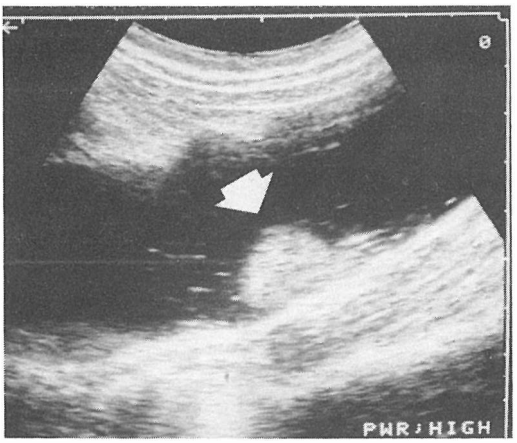

Figure 3. Sessile polyp (arrow).

Discussion

From the above results it can be seen that colonic sonography is the most useful clinical diagnostic procedure. It is non-invasive and easily carried out by means of a real-time ultrasound apparatus and a 5 MHz probe. The scan of the colonic wall is reliable, showing pathological changes in the wall and their expansion into the vicinity of the colon, as well

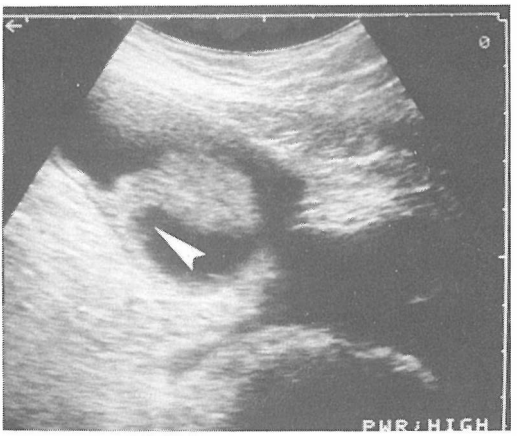

Figure 4. Polyp on a narrow stalk (arrow).

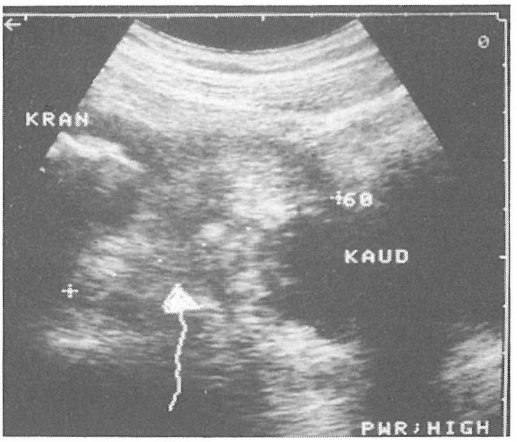

Figure 5. Polypoid colon carcinoma.

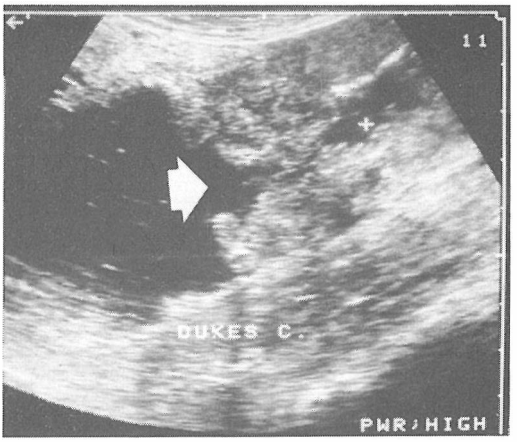

Figure 6. Stenotic colon carcinoma (arrow).

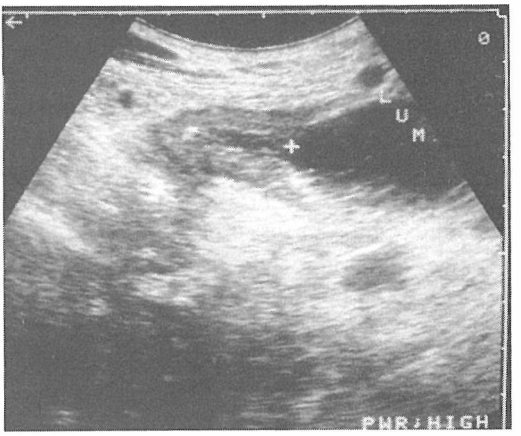

Figure 7. Crohn's disease – stenotic section.

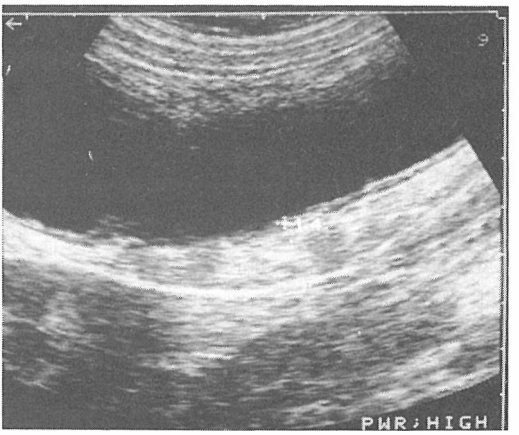

Figure 8. Ulcerative colitis – swollen wall.

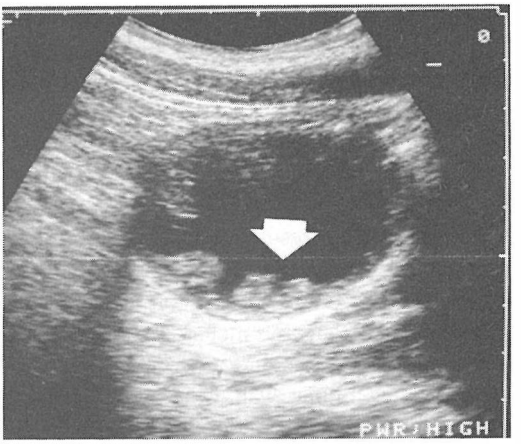

Figure 9. Ulcerative colitis – pseudopolyp (arrow).

as the length of the afflicted section of the bowels. From the results obtained so far we can draw the following conclusions:

– the sonography scan of the colonic wall is up to 5 mm thick and consists of five layers (Figure 1)

– with normal findings, from the lumen of the colon which appears dark (anechoic) small movable hyperechoic lamelliform plates protrude (Figure 2)

– polyps on stalks or broad bases stand out in the lumen appearing as oval echoic formations; the wall at the base the polyp is of normal structure (Figure 3 and Figure 4)

– the colon carcinoma prominent in the lumen is of irregular surface and does not float in the lumen, has no peristalsis, and at the touch of the probe remains unchanged (Figure 5)

– stenotic carcinoma infiltrates the wall, thus narrowing the lumen, is of irregular echo structure with irregular surface of the colonic wall (Figure 6)

– part of the colon affected by Crohn's Disease is extremely swollen, the lumen is narrowed, the layers of the wall are not discernible (Figure 7)

– parts of the colon affected by ulcerative colitis show hypoechoic moderately swollen wall; the wall is clearly discernible, but there is no haustra and the lumen is not stenotic.

These conclusions basically agree with those reported in the available literature.[8–14]

In the group of patients treated, the sensitivity of the method amounts to 94 %, confirming the assertion of the applicability of this method in everyday routine and representing a stimulus for further improvements. Self-evidently, in particular cases it is necessary to use also other supplementary methods such as colonoscopy. It is particularly encouraging that surgical findings have, with the exception of one case, confirmed the colonic sonography findings on the extent of colon carcinoma.

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The role of radiation in the treatment of childhood malignancies

Berta Jereb

Institute of Oncology, Ljubljana, Slovenia

Improvement in the cure of childhood malignancies in the last decades has mostly been due to chemotherapy, however, this modalitity alone is unable to cure solid tumors; there, radiation treatment is an essential part of therapy, especially when surgery is not feasible.
The treatment of malignant tumors in children is therefore often combined: surgery, radiation and chemotherapy may be used sequentially or simultaneously.
At present we are still gathering new information about the timing of radiation, the curative tumor doses, the tolerance of normal tissue when radiation is combined with chemotherapy. The late effects of combined treatment remain a major problem, increasing with the time of observation. These considerations are crucial in children who are more susceptible to radiation damage and have a longer time to develop sequelae and live with them.
Regular follow-up with psychosociaal, endocrinological and cytogenetic aspectst have to be evaluated in detail in children treated for malignancies.

Key words: neoplasms-radiotherapy; child

Introduction

Ionizing radiation has been a part of cancer treatment virtually since its discovery by the Curies and W. C. Roentgen about 90 years ago. In sufficient doses it will kill normal as well as malignant cells and its clinical effect is based on the generally greater sensitivity of the latter. While it is used in some benign conditions, its beneficial effect in patients with malignant tumors has been well recognized.

Correspondence to: prof. Berta Jereb, MD, Ph. D., Institute of Oncology, Zaloška 2, 61000 Ljubljana, Slovenia.

UDC: 616-006.6-053.2:615.849.2

The treatment of malignant tumors in children is often combined: surgery, radiation and chemotherapy may be used sequentially or simultaneously.

Although the dramatic improvement in the cure of childhood malignancies in the last decades has mostly been due to chemotherapy, this modality alone is unable to cure solid tumors. Radiaton treatment is an essential part of treatment of these, especially when surgery is not feasible (Figure 1).[1]

If the choice is radiation treatment with attempt to cure, this goal should be pursued vigorously, taking into account some degree of complications, since the issue here is life. After deciding whether curative or palliative radiation therapy is indicated, the dose, volume, and

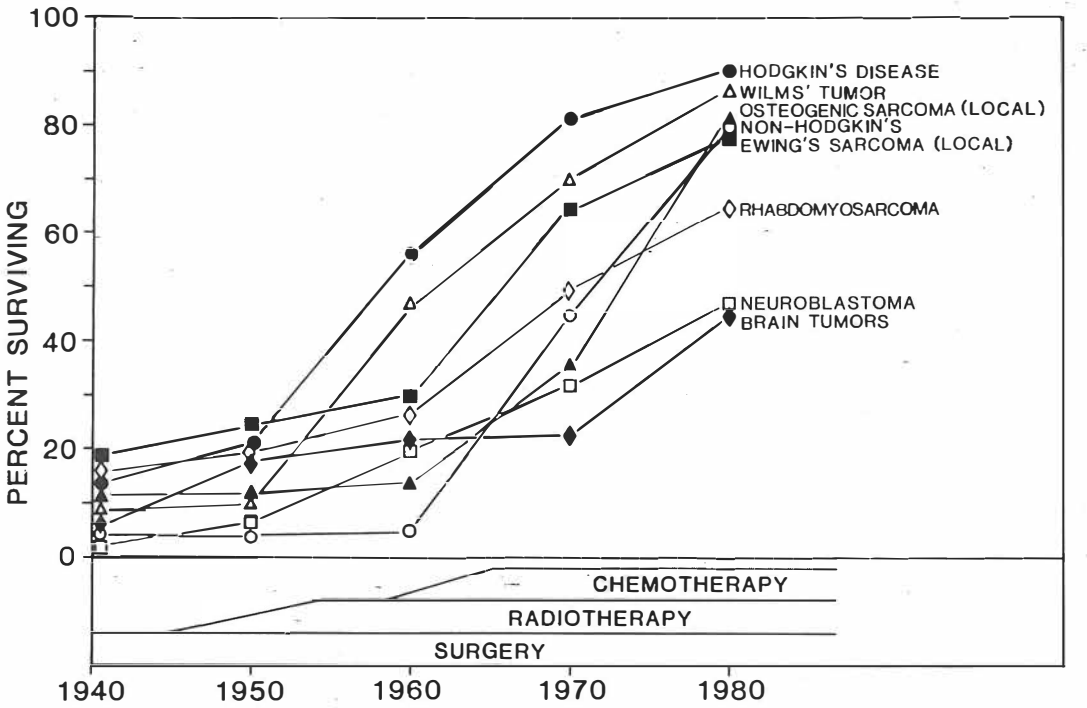

Figure 1. Improvement of 2-year survival of children with malignant tumors during the decades when surgery, radiation therapy, and chemotherapy were developed as a combined modality therapy (1940–1980) – Hammond 1986.

time during which it is delivered are determined.

Some radiobiological and technical aspects

Although radiation affects all parts of the cell, the inhibition of mitotic activity is its most important feature. Rupture of chemical bonds within the DNA molecule strands occurs either by direct absorption of radiation, or indirectly, by ionization of H_20 producing active radicales and electrons.

Microscopical changes are essentially the same, whether the irradiated cell is normal or malignant. The radiosensitivity of a malignant tumor tends to be in the same range, though usually at least somewhat higher, than that of the tissue from which it arose. Thus, tumors, arising from bone marrow, lymphatic tumors, and seminomas, tend to be very radiosensitive, while those arising from cartilage, bone, connective and neural tissues are much more resistant to radiotherapy. The radiocurability will depend, among other factors, on the radiosensitivity of a tumor and the tumor site, limiting the dose of radiation tolerated, as well as on the tumor size.

In order to increase the selectivity of radiation we can:

1) plan such a dose distribution that will result in a low dose (below the tolerance level) for normal tissue and a higher dose (tumoricidal) to the tumor. An adequate image of the treated area, often at several angles, is necessary for planning. A CT scan is usually helpful (Figure 2).

2) increase the gap between the effect on tumor cells and normal cells by fractionation (Figures 3a, 3b, and 3c).[2, 3]

In general, protracted fractionation is used over several weeks, with about 1000 cGy delivered each week. Recently, attempts were

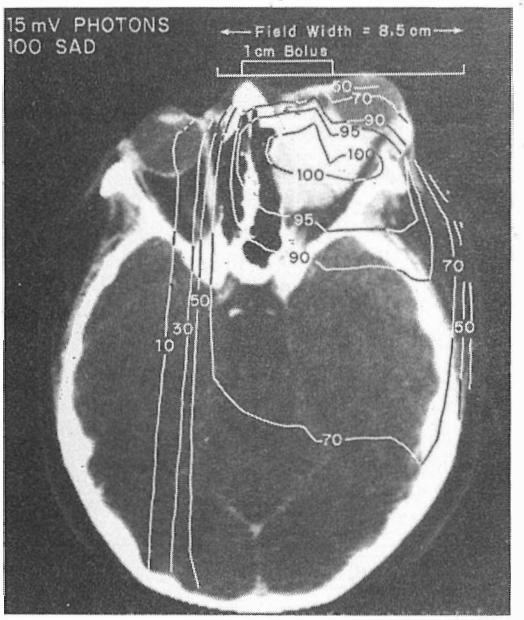

Figure 2. Treatment plan (isodose distribution) for a patient with embryonal rhabdomyosarcoma of the orbit.

made to base the fractionation scheme on modern radiobiologic research, using 2 or 3 daily fractions. Ideally, the dose and its distribution should be timed with the individual tumor growth, but we still lack the knowledge to achieve this (Figures 4, 5).[2]

3) moodify the effect of radiation with radiosenzitizers and radioprotectors (Figure 6).

Various physical, chemical, and biologic agents can modify the radiation response of the cells. Antimetabolites, such as Methotrexate, 5-fluorouracil, and 6-mercaptopurine, also interfere with the DNA synthesis. Cells exposed to these agents become more sensitive to radiation.

Clinical aspects of radiotherapy

Radiation therapy can be given:

locally:
- directly to the tumor (radiosensitive), to inoperable tumors: e. g. ERMS of the epihparynx,
- postooperatively to the tumor bed e.g. Wilms' tumor, Ewing's sarcoma)
- preoperatively, although it has been mostly replaced by chemotherapy it is still used when the response to chemotherapy is poor e.g. neuroblastoma)

or sistemically:
- TBI (total body irradiation) and
- HBI (hemibody irradiation).

It can be given after, before or sandwiched between chemotherapy (e.g. Hodgkin's lymphoma).

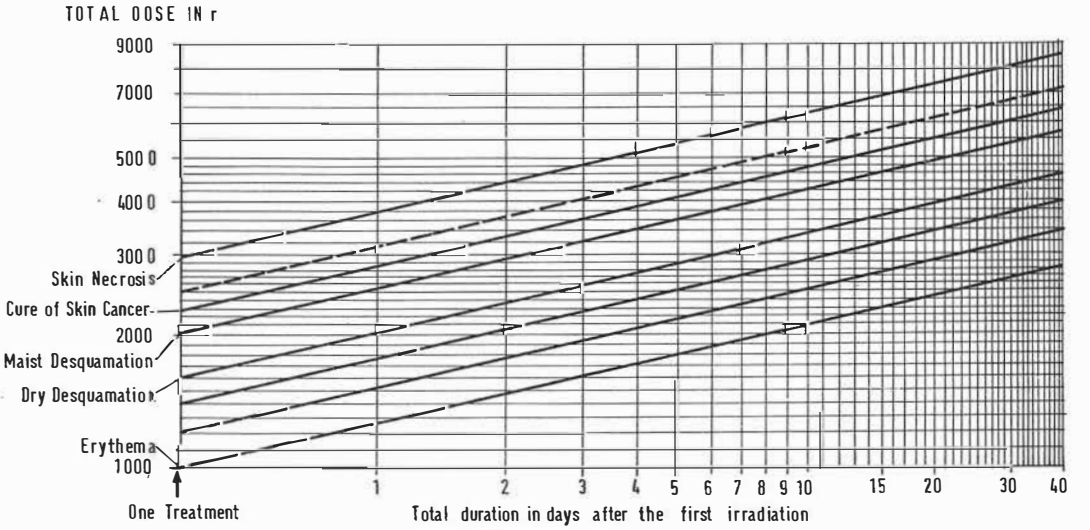

Figure 3a. Effect of fractionated radiation on tumor and normal cells – shematic presentation.

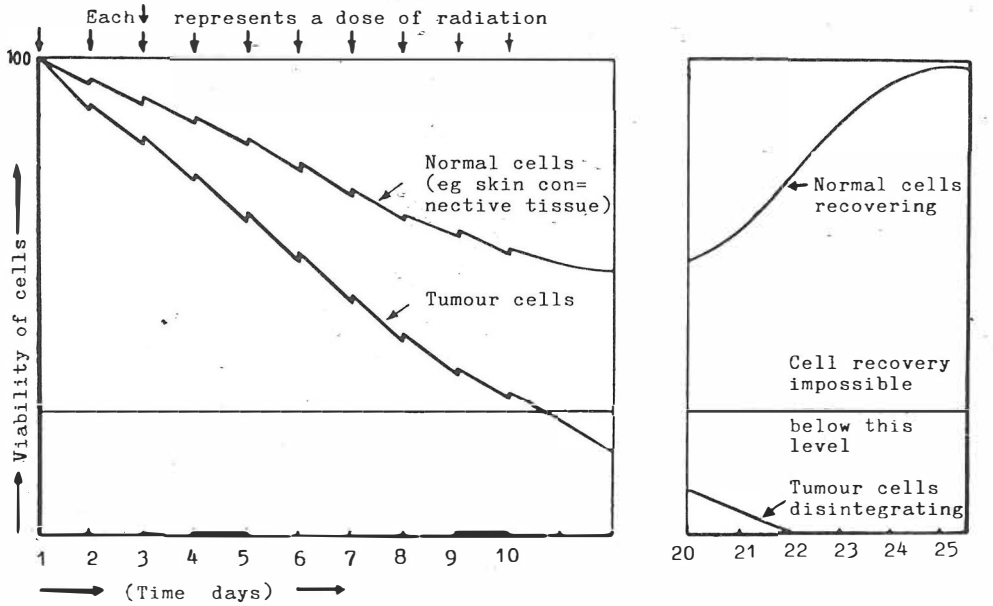

Figure 3b. Effect of fractionated radiation on tumor and normal cells – shematic presentation.

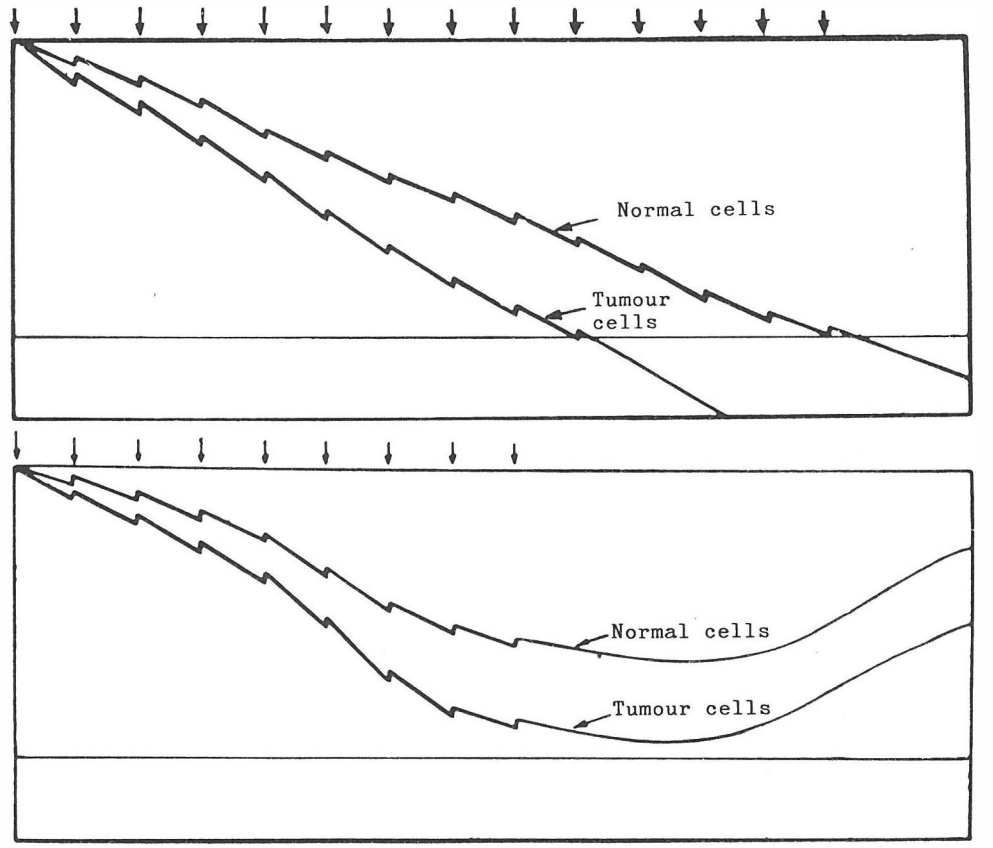

Figure 3c. Effect of fractionated radiation on tumor and normal cells – shematic presentation.

The main sources of radiation used in clinical practice are either external beam machines or sealed radioactive sources. External beam machines emanate:

photons (X-ray machines, betatrons, linear accelerators),

gamma-rays, (Co60 machine, teratron, gammatron, etc.)

electrons: betatrons, linear accelerators protons, neutrons are still only seldom used.

The advantages and disadvantages of different sources can be understood by comparison of the absorbtion of radiation in tissue presented by the isodose distribution courves (Figure 7).

The amount of irradiation prescribed is expressed in units, i.e., the quantity of energy absorbed by unit of mass (ergs/per gram). Rad is the unit absorbed dose where:

1 rad = 100 ergs/gram

A special name for the unit of absorbed dose

is Gy where

1 Gy = 100 rad.

Radiotherapy treatment planning is a routine procedure, and significant improvements are unlikely to occur in the near future. The difficulties, however, are still on the medico-clinical side, e.g. how to specify the targer volume occupied by the tumor bearing tissue more accurately.

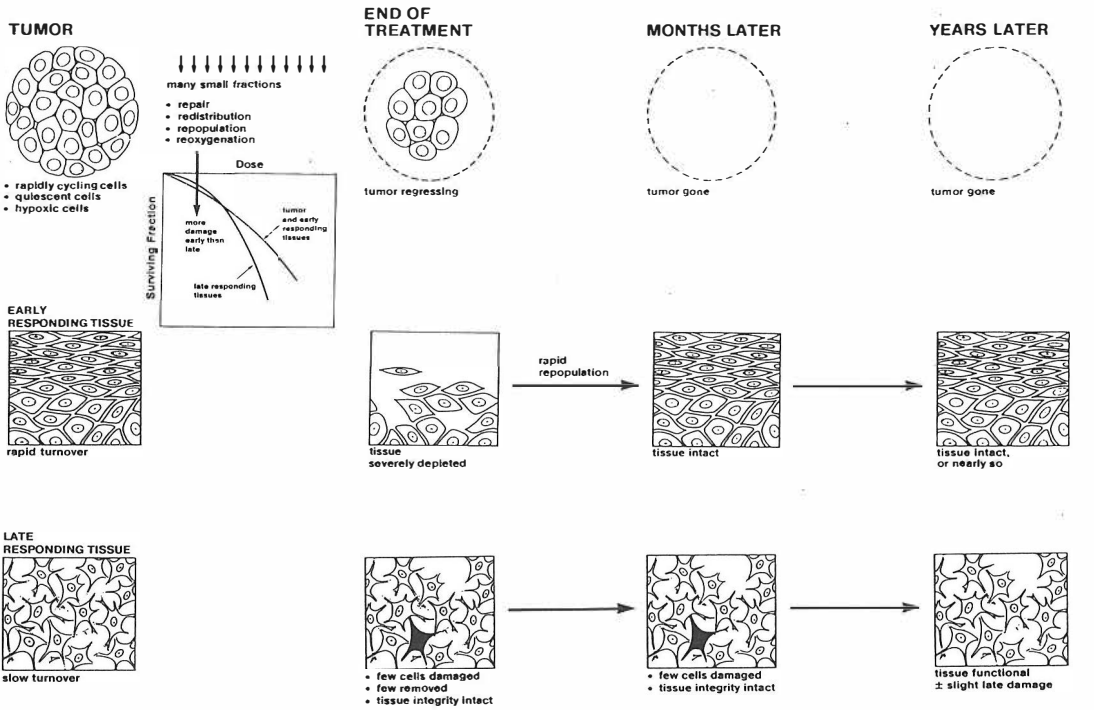

Figure 4. The kinetic pattern following irradiation with many small dose fractions. A small dose fraction produces relatively less damage to late-responding that to early--responding tissues because of their curvy dose-response relationship. The tumor regresses and disappears. The early-responding tissues show a reaction but repopulate by rapid cell division. The late responding tissues show little damage.

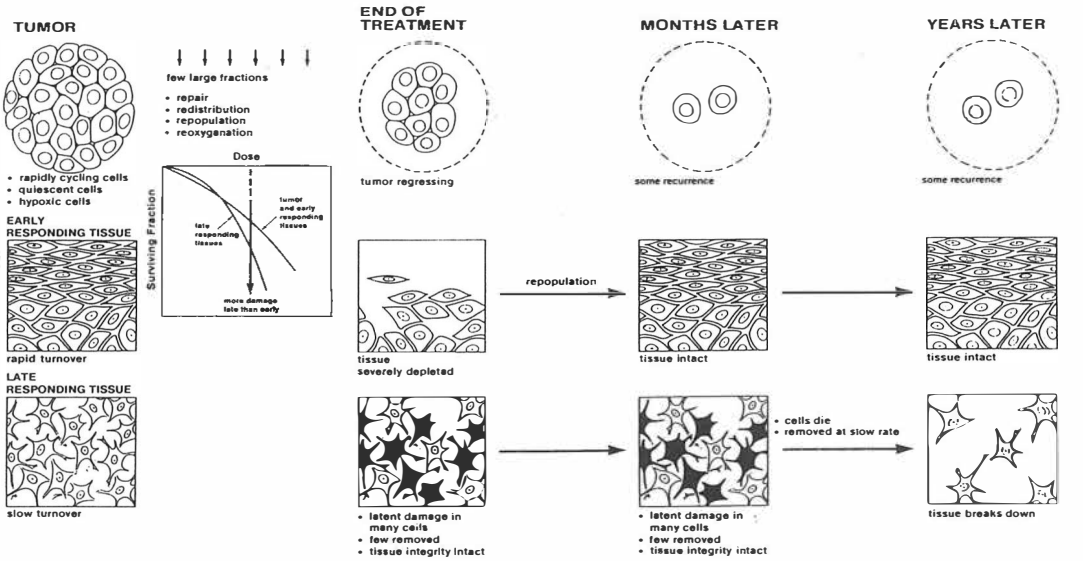

Figure 5. The kinetic pattern following irradiation with a few large dose fractions. A large dose fraction produces relatively more damage to late-responding than to early-responding tissues because of the difference in curviness of the dose-response relationship. The tumor regresses and disappears, though there is evidence of a higher recurrence rate after radiotherapy regimens involving a small number of fractions, perhaps because there is less opportunity for reoxygenation. The early-responding tissues show a reaction but repopulate by cell division; this is the same as in Figure 4 and 5. However, the late responding tissues carry a large amount of latent damage which is expressed months or years later when the cells in these tissues begin to turn over.

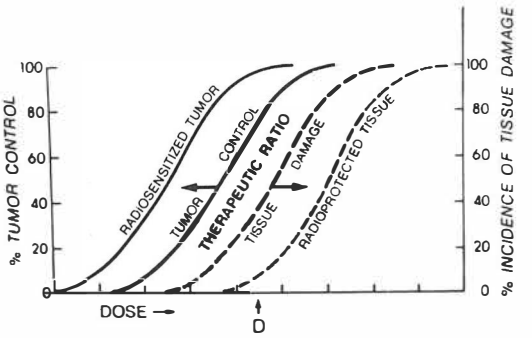

Figure 6. Scheme of therapeutic ratio modification.

Rather than in radiotherapy treatment planning, advances are likely to occur in areas such as combination regimens and modification of dose fractionation schemes. Also, as the prognosis is related to the extent of disease at the beginning of treatment, an earlier diagnosis is essential together with a better knowledge of the spread, and patterns of failure of different tumors. Chemotherapy is an integral part of treatment in the great majority of tumors in children (Figure 8).[4]

Knowledge on the effects of such combined treatment has accumulated very rapidly in the last decades; it is likely, however, that in the near future, we shall still be gathering new information about the timing of radiation, the curative tumor doses, and the tolerance of normal tissue when radiation is combined with chemotherapy.

Although the acute radiation effects (even severe when ChT is given concomitantly) on normal tissue may resolve rapidly, the late effects of radiation remain a major problem, increasing with the time of observation. These considerations are crucial in children who are more susceptible to radiation damage and have a longer time to develop sequelae and live with them (Figure 9).[5]

Some late sequelae have not been recognized until recently and some may be more common

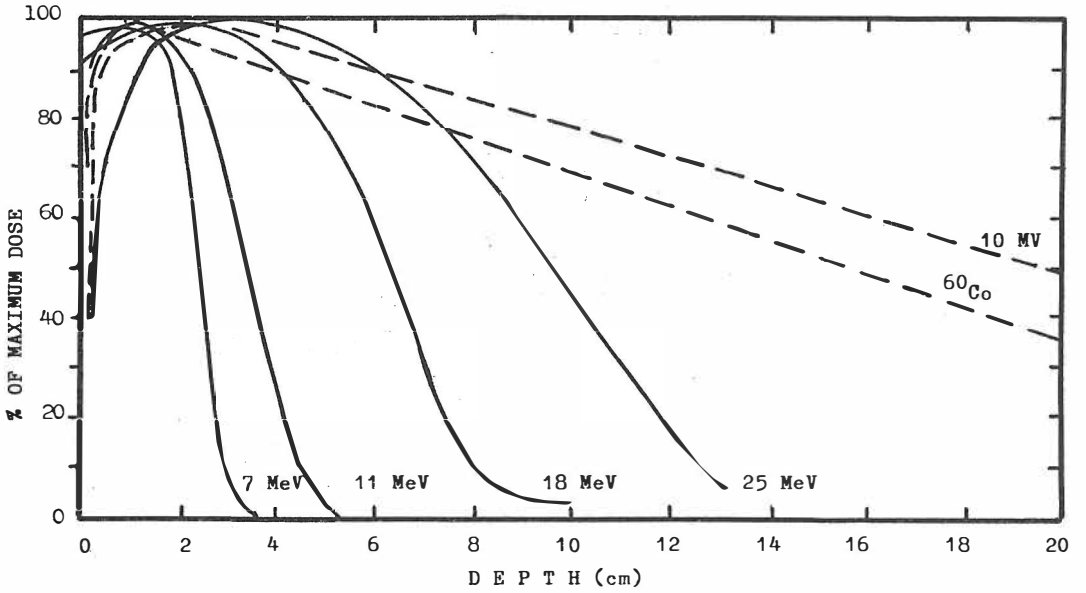

Figure 7. Central-axis-depth dose curves for electron and X-ray therapy beam.

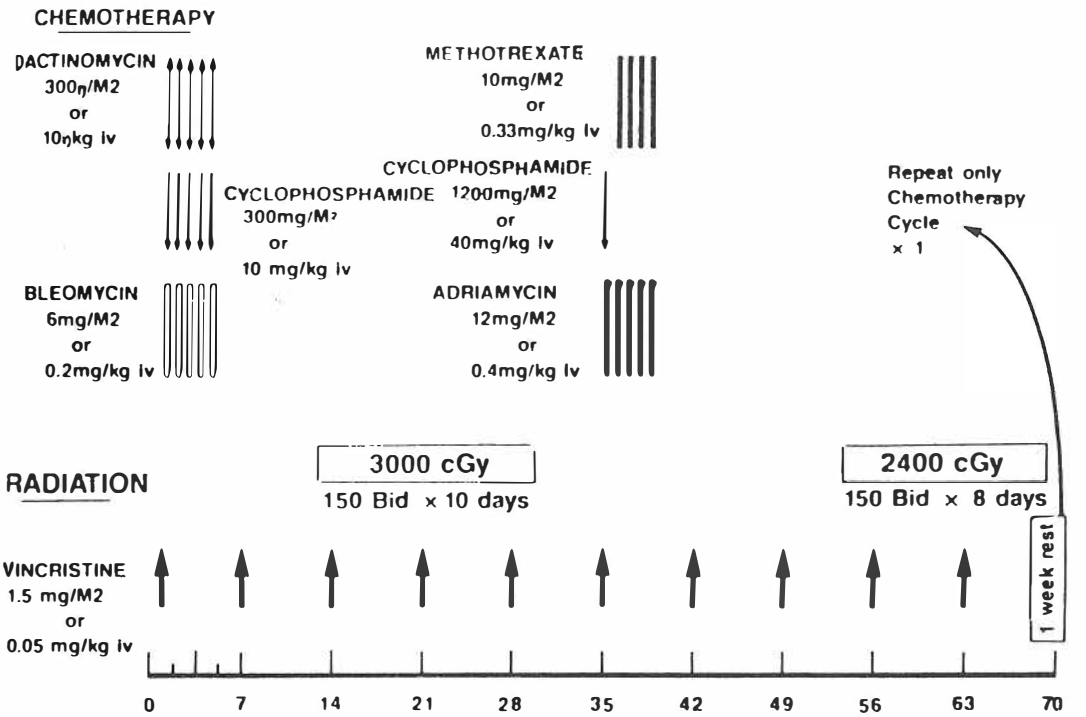

Figure 8. Multidiscipline protocol for solid tumors (Memorial Sloan-Kettering Cancer Center).

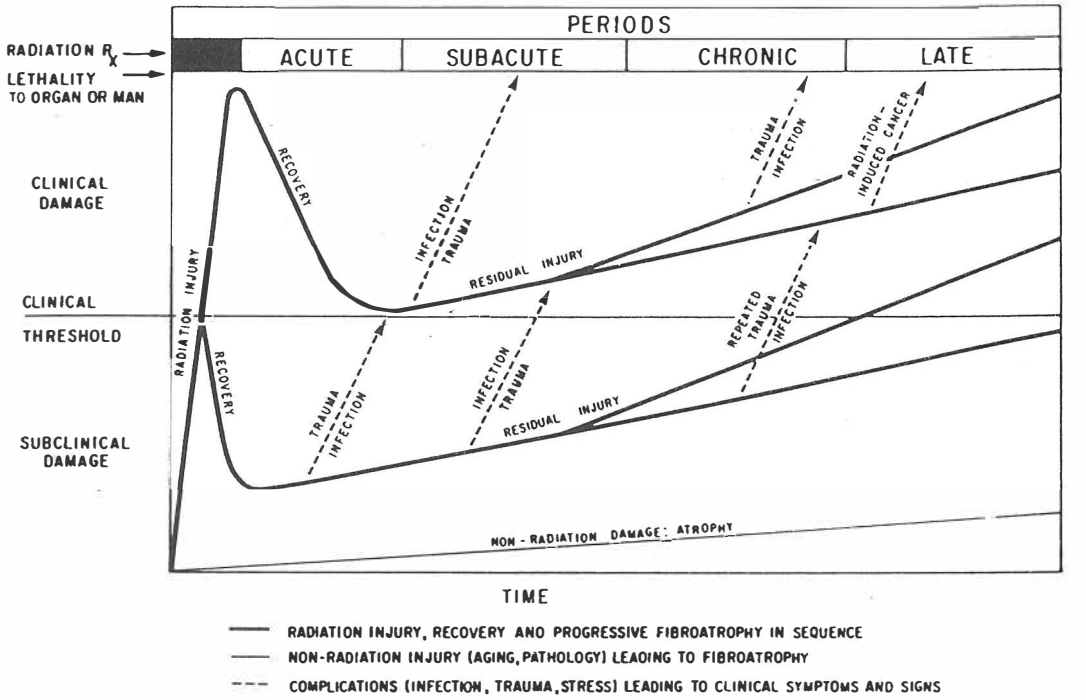

Figure 9. Clinicopathological course of radiation effects: general scheme (Rubin 1968).

than appreciated in the past. While our predominant concern some decades ago was to save the life of the afflicted child, it is now becomming equaly important to minimize the treatment sequelae.[6] Regular follow-up including detailed psychosocial, endocrinological and cytogenetic investigations is required in children treated for malignancies.[7] It has been recognized also that some sequelae can be effectively treated or compensated for. Even secondary tumors, the most serious of the consequences, can be successfully treated if recognized in time.

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Inflammatory breast cancer
Five-year survival of patients with inflammatory breast cancer treated in the period 1986–1987 at the Institute of Oncology in Ljubljana

Jurij Lindtner

Institute of Oncology, Department of Surgery, Ljubljana, Slovenia

A review of five-year survival of 35 patients with inflammatory breast cancer treated at the Institute of Oncology in the years 1986–1987 is presented. The initial and basic systemic therapy was complemented by surgery and/or irradiation. Five year survival was 11 %, and the median duration of survival 23 months.

Key words: breast neoplasms-therapy; survival analysis

Introduction

The introductory words of different reports on inflammatory breast cancer (IBC) are incredibly alike: they invariably comprise the following two statements:

– IBC is "the most malignant malignoma" of the breast,

– IBC is a rare disease representing 1-4 % of all breast cancers.[1,2]

The fact that this is a special breast disease was noted by Bell already in 1807; he regarded the pink skin with underlying breast tumor a very bad prognostic sign.[3] By the end of the previous century, Billroth and Volkman found a name for the disease: they called it "mastitis carcinomatosa", and the term has remained in use till present days.[2] In 1889, Bryant described a carcinomatous infiltration of the subcutaneous lymph vessels – a phenomenon which has been found diagnostically relevant.[4]

The first detailed description of IBC was given in 1911 by Schumann. In 1924, Lee and Tannanbaum named the disease inflammatory breast cancer.[1] The obsolete names such as mastitis carcinomatosa, carcinoma mammae acutum, carcinoma mastoides have gradually been abandoned. The authors completed the description by yet another observation: "The inflamed skin areas are sharply delineated as in erysipelas.[1] In 1971 Haagensen noted that" in advanced form of IBC the whole breast is enlarged and hardened, whereas the overlying skin is erythematous and swollen.[2]

In 1974, Salzstein declared IBC to be a pathomorphological diagnosis, and introduced the phenomenon of "hidden (i.e. clinically occult) IBC".[1] In 1978, Lucas and Perez-Mesa,

Correspondence to: Assoc. Prof. Jurij Lindtner, MD, PhD, Institute of Oncology, Department of Surgery, 61105 Ljubljana, Slovenia.

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using the data on median survival of patients with IBC, tried to clarify whether IBC was a clinical or a pathomorphological diagnosis:

Diagnosis	Median survival
Clinical only	14 mos
Pathomorphological only	40 mos
Clinical and pathomorphological	16 mos

These data are in agreement with the presently prevailing belief that the diagnosis of IBC is clinical.[4]

According to the presently valid definition of the International Union Against Cancer (UICC/AJC-1986), IBC is "diffusely thickened and hardened breast skin with erysipeloid margins, and generally without a palpable tumor".[5]

A distinction should be drawn between two different forms of IBC: 1) the true IBC is characterized by an acute onset and simultaneous involvement of most part of the breast, frequently without a palpable tumor – called also classical or diffuse IBC (DIBC), and 2) the "neglected" breast cancer with a protracted anamnesis, an apparent tumor and visible signs of inflammation in the affected quadrant of the breast – also called localized IBC (LIBC). The differing data on the survival of patients with IBC could be explained by this double nature of the disease. Therefore in 1956 Haagensen warned that "the diagnostic criteria are interpreted too liberally, and as a result we may jump to a conclusion on diagnosis too quickly".[6]

With respect to TNM classification, the greatest prognostic relevance should be attributed to the factors N and M. The fatality of IBC correlates with the growth of N from N0 to N3, and from M0 to M1. A good response to an initial systemic therapy can be regarded as a favourable prognostic sign. However, the "neglected IBC, i.e. LIBC, with its protracted anamnesis and signs of inflammation limited to a part of the breast, is associated with quite a different prognosis then DIBC. "*Peau d'orange*" and mammographic evidence of thickened skin are certainly among unfavourable prognostic signs.[7] Thus, the following three prognostic categories can be distinguished:

Favourable – LIBC N0-1
Moderate LIBC N2-3; DIBC N0-1
Unfavourable – DIBC N2-3.[8]

Self-evidently, the above distribution is applicable only in patients with IBC and no clinical evidence of metastatic spread at the time of diagnosis (M0).

The presented analysis is the most recent report on the survival of patients with IBC treated at the Institute of Oncology in Ljubljana, during the first five years after the beginning of therapy.

Materials and methods

Our review of the course of IBC comprises the data on patients who commenced treatment at the Institute of Oncology in Ljubljana, during the years 1986–1987. Such a selection of patients enabled us to assess their 5-year survival results.

In the appointed 2-year period, 1227 new breast cancer patients were registered by the Cancer Registry of Slovenia.[9,10] In the same period, Hospital Registry of the Institute of Oncology in Ljubljana registered 1278 new breast cancer cases. The difference in the total numbers of new cases can be attributed to the fact that there were also some patients from other former Yugoslav republics treated at the Institute in Ljubljana.

According to the data of the Hospital Registry for the years 1986–87, 149 of newly registered breast cancer patients were permanent inhabitants of Slovenia, who were admitted to the Institute of Oncology in Ljubljana for the treatment of breast cancer classified as T4. Here, the beginning of treatment is explicitly stated because of the already mentioned Haagensen's warning on a vague diagnosis of IBC as a rare disease, whereas the emphasis on permanent inhabitants of Slovenia results from the fact that in the last few years, the data on the course of disease have been available only for patients permanently living in Slovenia.

A riview of medical records on these 149 patients with "T4" breast cancer revealed that there were only 35 among them with classical (difuse) T4d IBC (23%), and their course of disease is the subject of this report.

Results

The age distribution of the studied patients is evident from the following table:

Table 1. Age distribution.

Range	30–65 years
Mean age	51 years
Median	49 years

Table 2 shows the frequency of left or right breast involvement in our group of patients:

Table 2. Affected breast.

	No. of pts
Left	25
Right	9
Both	1
Total	35

The distribution of patients according to TNM classification was as follows:

Table 3. Distribution by TNM.

N	M	No. of T4d pts
NO	MO	3
N1	MO	16
N2	MO	5
N3	MO	6
NO-3	M1	5
Total		35

The treatment of the patients included in our study is presented in Table 4:

Table 4. Distribution by the type of initial therapy.

Treatment modality	No. of pts
Systemic	1
Systemic + irradiation	13
Systemic + surgery	2
Systemic + irradiation + surgery	6
Systemic + surgery + irradiation	13
Total	35

Discussion

IBC is not just a severe, so far insoluble therapeutic problem. The difficulties start already at the time of diagnosis. The opinions of different authors cited in the Introduction are in agreement with this statement. Here again the attention should be called to the Haagensen's description where the author states that "when sufficiently advanced", the disease is not difficult to identify. Also the hardening and enlargement of the affected breast can be regarded as diagnostically relevant clinical signs, whereas the skin edema is already questionable; TNM classification (1987) provides the following definition:

T4a – spread to the chest wall

T4b – edema (including *peau d'orange*) or ulceration of the skin of the breast, or satellite skin nodules confined to the same breast

T4c – both 4a and 4b, above

T4d – inflammatory carcinoma.[5]

A demanding reader would find this definition rather vague.

It is quite easy to interpret a skin edema as an early sign of IBC, particularly when it is associated with mammographically evident thickening of the skin. On the other hand, a total breast involvement can hardly be regarded as conclusive for IBC. The fact that some patients are first seen with already advanced disease suggests that these patients themselves "took care" of the disease in its early stage, though this phase might not have lasted well over a few weeks, considering the rapid course of the disease. It is also possible that some patients do see doctor sooner than others. In such cases the symptoms of the disease are less expressed, and limited to a single quadrant of the breast. Therefore, IBC should be searched also among breast carcinomas classified as T4b. The same ambiquity is associated also with the next important sign, i.e. erythema: this can be attributed either to carcinomatous dermatolymphangiosis or to aspetic inflammation due to central necrosis of a slowly growing breast cancer. The frequent tendency to interpret these two "red"

breast cancers as one and the same entity just proves how difficult it is to draw a distinction between the two different types of erythema. This statement can be substantially confirmed by numerous reports in foreign literature, as well as by our own studies. Last but not least, the unreliability of clinical detection of the disease is best confirmed by the opinion the IBC is a pathomorphologic and not a clinical diagnosis. However, since clinical identification of the disease cannot not be avoided, we should strive to improve it through upgrading of experience. Such an approach might prevent us from misinterpreting some quackery-related inflammation for IBC.

Though *our group of presented patients* may seem small, when compared with groups of IBC patients reported by other authors, it can be assessed as medium-sized. Besides, it should be taken into account that only the patients with classical diffuse IBC were included, which is also reflected in their age distribution. Namely, there are no older patients in our group. The patients age reported in the literature ranges from 25 to 84 years, though the youngest known patient was only 12 years old.[4] Localized IBC is generally seen in older patients which, however, have been omitted from our analysis.

According to the data of the Cancer Registry of Slovenia, the incidence of IBC in our country is within the range of medium values reported in the Introduction: 35 observed patients among 1.227 evidenced by the Registry represent 2.8 % of all breast cancers. This rate is fairly reliable, considering that most patients with advanced and disseminated breast cancer start their treatment at the Institute of Oncology (a review of medical records suggests that perhaps one or two patients with IBC have started their treatment elsewhere). Taking into account all probable IBC patients, the number amounts to 3 % of all breast cancers.

We have no evidence of male patients with IBC, though according to the data from literature such cases do exist.[11]

The results of foreign and own investigations show that breast cancer equally frequently affects each breast (a slightly more frequent involvement of the left breast is negligible). In our group of patients with IBC this rate was 26 vs. 10 in favour of the left breast (taking into account that a patient with bilateral involvement was considered in both groups). According to the foreign experience, IBC is almost twice more frequent in the left than in the right breast.[12]

Our data on the *treatment* of the observed patients are scanty, and so are also the reports on these patients and their disease; namely, in one fifth of the cases the primary patient record could not be found. Therefore, the data that could be collected on the treatment of our group of all 35 patients have been presented in Table 4.

The information reveals, however, that all the patients under study received systemic therapy. This is in agreement with presently respected principles on the treatment of IBC. For the sake of comparison, I am giving below some data in on the survival of patients before the use of systemic therapy that have been reported in the same publication.[4]

a) *Surgery alone:*
- mean survival 21 months
- 19-month average survival reported by Haagensen
- 3.5 % five-year survival reported by Treves

b) *Radiotherapy alone:*
- mean survival 14 months

c) *Surgery and radiotherapy:*
- mean survival ranges between 7–29 months;
- only Perez and Fields (1987)[4] reported a 42-month average survival of patients treated by the combined approach.

The use of systemic therapy considerably prolongs the average survival, regardless the type of local therapy (if any was used at all): mean survival reported in the literature ranges between 23.6 and 46 months.[4] Mean survival results of our patients (23 months) are therefore slightly below the above cited values. Perhaps this fact could be attributed to our already mentioned strict criteria for patient selection. Figure 2 presents two data on mean survival: thus prognostically favourable group survived 31 months and prognostically unfavourable

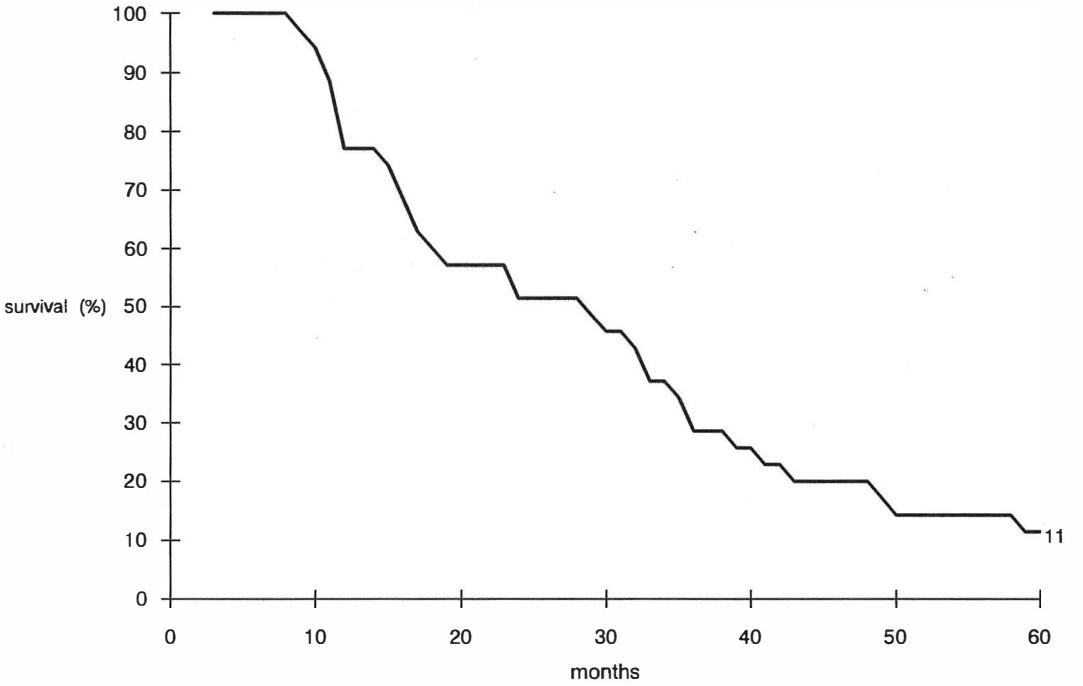

Figure 1. Curve of actual survival results in 35 patients with IBC.

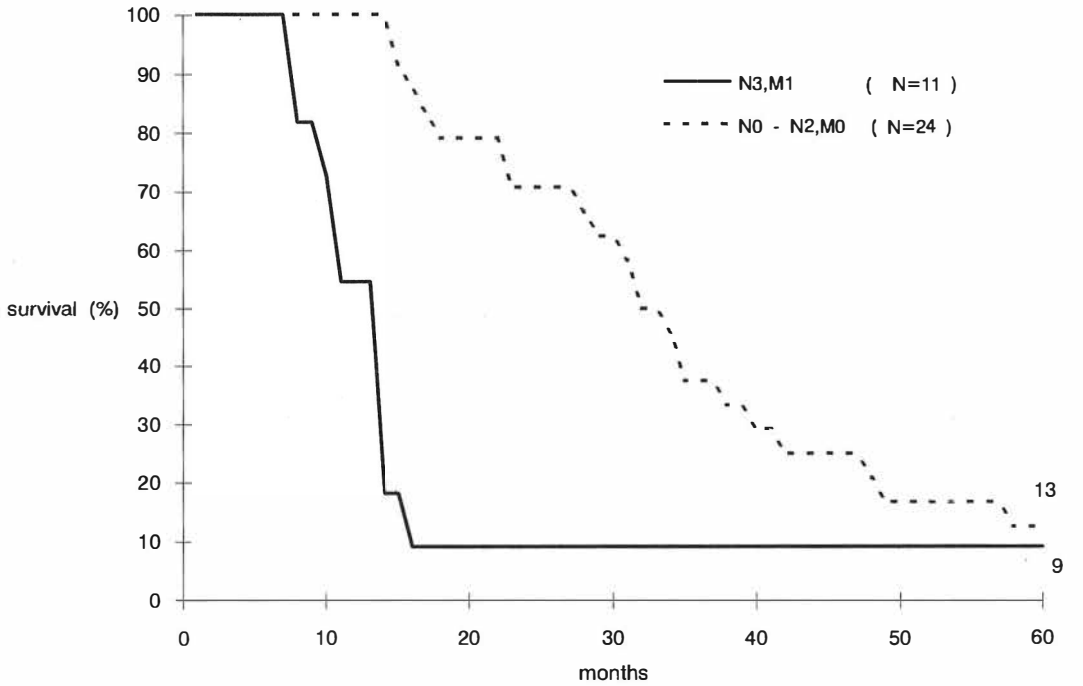

Figure 2. Curve of actual survival results in 35 patients with IBC, distributed into 2 prognostic groups.

group 14 months on average. Graph 2 also shows 5-year survival of a patient form prognostically unfavourable group (N3, M1) which could be attributed to vague clinical classification.

The data on 270 patients with IBC M0 reported by Institute Gustave Roussy[13] are as follows:

– 28% *five-year survival* of patients treated by *irradiation* (and castration when fertile);

– 40% *five-year survival* of patients treated by systemic therapy according to AVM schedule (adriamycin, vincristine, methotrexate) and maintenance chemotherapy with VCF (vincristine, 5-fluorouracil, methotrexate and endoxan).

In comparison with the patients mentioned above, only 11% five-year survival has been observed in our patients with IBC M0. Owing to the incomplete information on forms of systemic therapy no other conclusion can be drawn apart from that general observation. We should be aware, however, that any detailed analyses of this topic based on uncontrolled, non-randomized retrospective studies such as ours can be done only exceptionally and are, as a rule, not feasible.

Conclusion

Here I would repeat the initial statement: IBC is a tough diagnostic as well as therapeutic problem which is somewhat underestimated because of its rare occurrence. This cognition could represent a stimulus for further studies.

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Radiol Oncol 1992; 26: 326-32.

The history of nuclear medicine in the Republic of Slovenia II – spread of the new medical speciality into peripheral hospitals from 1960 to 1974

Janez Šuštaršič

Institute of Oncology, Ljubljana

The second part of this historic overview describes the establishment of five hospital departments of nuclear medicine in the regional hospitals of Slovenj Gradec (1960), Celje (1968), Maribor (1973), Šempeter near Gorica and Ankaran (1974). The Basic Laboratory for Work with Radionuclides in Ljubljana, which represented the origin of all nuclear medical activity in Slovenia in its earliest pioneering era, gave rise to the following two units: Department of Nuclear Medicine at the Institute of Oncology, and the Clinic of Nuclear Medicine at the University Clinical Center in Ljubljana.

For nuclear medicine, the 70's meant a period of rapid development induced by the introduction of radioimmune tests into the diagnostics in vitro, whereas the diagnostics in vivo was boosted by new devices such as gamma cameras, computers and Tc-generator. The number of new investigations has rapidly increased, and also the frequency of all investigations showed a trend of sharp increase all until 1980 when this progress slowed down. At that time diagnostics in vivo were implemented by ultrasonography and computerised tomography, whereas in the diagnostics in vitro radioimmune assays were gradually replaced by tests based on immunofluorescence and by other techniques which did not require radioactive labelling.

In the 80's, some investigations such as e.g. liver and kidney scintiscan were gradually abandoned in order to give place to some new ones (e.g. radionuclide ventriculography). The frequency of investigations after having reached its peak became stable, and annual frequency of investigations remained basically the same. A recapitulation from 1984 for the whole Slovenia with its population of 2,000,000 showed that a total of 44,215 investigations in vivo, 185,175 in vitro and 504 therapeutic applications of radiopharmaceuticals had been performed in that year in all seven Slovenian units of nuclear medicine.

Key words: nuclear medicine – history; Slovenia

Introduction

In the first part of this historic overview the development of nuclear medicine in the capital of Slovenia since its beginnings at the Clinic of Internal Medicine in Ljubljana (1954), through the period of their joint work under the shared roof of the Basic Laboratory for Work with Radionuclides (1960–1968), up to the moment when the internistic and oncological nuclear medicine have finally separated, is presented.

The second part of this historic overview

Correspondence to: Prim. Janez Šuštaršič, MD, Institute of Oncology, Zaloška 2, 61105 Ljubljana, Slovenia.

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describes the establishment of five hospital departments of nuclear medicine in the regional hospitals of Slovenj Gradec (1960), Celje (1968), Maribor (1973), Šempeter near Gorica and Ankaran (1974).

The article also gives information on staff situation and work performed in 1984; these data were collected by means of a questionnaire for the needs of the 4th Austrian-Hungarian-Slovenian Scientific Meeting on Nuclear Medicine, which was held on May 1985 in Ljubljana, on the occasion of the 30th anniversary of nuclear medicine in Slovenia.

1960 – Slovenj Gradec: General Hospital Slovenj Gradec, Unit of Nuclear Medicine

The first attempts to spread nuclear medicine outside Ljubljana can be attributed to I. Raišp from the General Hospital in Slovenj Gradec who introduced investigations of the thyroid with radioactive Iodine. The uptake of radioactive Iodine (131-I) in the thyroid was measured 2, 8 and 48 hours after the patient had ingested a test dose of 50 μ Ci 131-I-Naiodide; the activity in urine excreted during 0–8 hrs, 8–24 hrs and 24–48 hrs following test dose intake was also measured (Raišp and Burnik 1964).

As to the equipment, their working conditions were worse than of their colleagues in Ljubljana. In 1964, Simoniti et al.[3] reported that using radioactive iodine, toxic adenomas of the goiter were discovered in 6 patients treated at the General Hospital in Slovenj Gradec. The author pointed out that owing to the lack of a scintiscanner, the hot thyroid nodes were localized manually using a Geiger-Mueller's tube. The article of Raišp from 1968[4] comprises a scintigram of a thyroid node imaged by the help of radioactive iodine, thus proving that a scintiscan facility had already been available in Slovenj Gradec at that time.

In 1984, six-member staff of the unit for nuclear medicine headed by I. Raišp performed 1446 *in vivo* and 7212 *in vitro* investigations, and applied therapeutic doses of radioiodine in 10 patients.[5]

1968 – Celje: Health Center Celje, Center of Therapy of Internal, Contagious and Dermatologic Diseases, Department of Nuclear Medicine

The Laboratory of Nuclear Medicine in Celje was built and equipped already in 1967, whereas regular work there started a year later; F. Fazarinc, specialist in internal medicine, became the head of the unit. Two of the staff members obtained their basic knowledge at the Institute "Boris Kidrič" by attending a course on the use of radionuclides in medicine. Additional practical and theoretical upgrading of their knowledge was accomplished later on at the Institute of Nuclear Medicine in Ljubljana.[6]

According to F. Fazarinc, further development of their laboratory and all advances in the quality of work occurred as a results of new equipment purchase. Thus the initial facilities were enhanced by kinetograph with analogous subtractor which was developed by the Institute Jožef Stefan; from that machine later on the team of J. Šnajder in collaboration with F. Fazarinc from Celje and M. Erjavc from the Institute of Oncology in Ljubljana developed a renograph. This has become a constituent part of equipment in numerous laboratories of nuclear medicine in former Yugoslavia. The purchase of a gamma camera DYNA 11/4 (Picker) with a computer PDP 11/34 (Digital) in 1978 denotes the next important mile stone in the development of nuclear medicine in Celje.

In 1984, 15 professionals headed by F. Fazarinc performed 5995 *in vivo* and 43,669 *in vitro* examinations, and applied therapeutic does of radionuclides in 17 patients.[6]

1968 – Ljubljana: Clinic of Internal Medicine, Department for Nuclear Medicine

The year 1968 means the end of the mutual work of specialist in internal medicine and oncologists in the Basic Laboratory which was situated in the former St. Peter's Military Barracks. The former moved into the Clinic of Internal Medicine, where upon the Laboratory of nuclear medicine changed its name and became a Department for Nuclear Medicine of

the Internal Clinic. In 1970 there were 7500 measurings performed in that department comprising 2 chemical laboratories, 3 measure rooms, one outpatient facility and one hematologic laboratory.[7, 10]

The Department, however, occupied that place only for a short period of time. Already in 1971 it moved in the 5th floor of the newly built Clinical Center in Ljubljana, though the construction works had not been completed yet. After having gained its organizational independence, the department became the **Institute of Nuclear Medicine.** This was the first institution in Slovenia to have a gamma camera PhoGamma III Nuclear Chicago with scintigraphic data analyser (computer) which was a prerequisite for introducing of new techniques in nuclear medicine.[7]

Further promotion of the Institute took place with completion of the Clinical Center in 1973, when it was allocated its permanent place in the groundfloor of the new building. Having obtained also suitable hospital ward capacities, the Institute finally became the **Clinic for Nuclear Medicine.** The staff consisted of 9 specialists in internal medicine, 9 graduated biotechnologists and 16 technical assistants. The Clinic functioned in three radiochemical laboratories with annual capacity of 20,000 competitive radiochemical examinations, and 5 rooms for *in vivo* measurements with annual turn over of 10,000 investigations. The data obtained by static and dynamic scintigraphy were quantitatively analysed by means of an electronic computer.[7]

Clinic for Nuclear Medicine was also a teaching base for two-term postgraduate study in nuclear medicine;[8] in 1974 the first ten students successfully completed their studies within the frame of this program. In the same year, a Section for Nuclear Medicine at the Slovenian Medical Society was established in Celje.[9] The Clinic became the seat of the Executive Board of the Section, as well as the seat of the Executive Board of the Yugoslav Society of Nuclear Medicine.

In 1975 the clinic – then already named the **University Clinic for Nuclear Medicine** – had a staff of 37 professionals. *In vivo* investigations were performed with two gamma cameras directly connected to two computers; a program computer was indirectly connected with a kinetograph (for kinetic measurements of renal and cardiac function) as well as with an automatic system for measuring of radioactivity in liquids. Programs for kinetic studies of renal, cardiac and cerebral function (vascularization), and for the analysis of radioimmune and other competitive radionuclide examinations *in vitro* as well as programs for computerization of scintigrams were performed.

With rapid development of the Clinic, discrepancies associated with the lack of space were brought to attention. Therefore, on the occasion of the 20th anniversary in 1975, a sanation program was accepted according to which the annual number of *in vivo* investigations should be reduced from 10,000 to 8,100, and *in vitro* investigations from previous 20,000 to 10,000; thus reduced program would be operative all until the Clinic's capacities would have been enhanced by new room capacities for out-patient service outside the existing ward. As a result, the sanation program did not so much decrease the extent of services performed, but rather stimulated the establishment of a new department for diseases of the thyroid, which found place in the basin of the Outpatient Clinic in Ljubljana. With this reconstruction in 1978, the Clinic for Nuclear medicine obtained a dislocated unit with 14 rooms for their outpatient activity.

In 1984, 52-member staff of the Clinic, headed by B. Varl, performed 11,961 *in vivo* and 107,636 *in vitro* examinations; therapeutic doses of radiopharmaceuticals were applied in 362 patients.

1968 – Ljubljana: Institute of Oncology, Unit of Nuclear Medicine

After dislocation of nucl. med. services for the needs of internal medicine, the rooms and equipment of the former Basic Laboratory were inherited by the **Department of Brachyradiotherapy and Nuclear Medicine of the Institute of**

Oncology. Further reorganization in 1970 split this service into two separate units, i.e. Brachyradiotherapy and Unit of Nuclear Medicine (UNM).

UNM primarily covered the needs of the Institute of Oncology.[10, 11] Apart from nucl. med. examinations, radionuclides were applied also for therapeutic reasons in patients with carcinoma of the thyroid, painful skeletal metastases and in patients with carcinosis of the serous membranes. The scope of work was never extended by *in vitro* investigations as in other nucl. med. laboratories in Slovenia.

While in the 70's all other units and laboratories of nuclear medicine in Slovenia used the equipment and radiopharmaceuticals commercially available in the country and abroad, and performed investigations that had already become a part of routine work elsewhere, at UNM the pioneer period was protracted well into the late 70's, which was reflected in perpetual experimenting and innovative activity.

A speciality of this unit, headed by M. Erjavec, was the development of own radiopharmaceuticals such as e.g. radioactive Fluor (F-18) by the help of school reactor TRIGA in Podgorica; labelling of Bleomycin with radioactive Cobalt (Co-57) and Technetium (Tc-99m). Further activity of this kind included "rediscovering" of certain investigations (e.g. perfusion scintigraphy using a neoport valve), in-house development of measuring equipment (e.g. whole-body scanner, renograph), and homemade computer programs.

Own Equipment:

Among *in vivo* investigations, the first place was taken by bone scintigraphy, first with radioactive Strontium (Sr-85), and later on, around the year 1970, with radioactive F-18. High energy of the used radiopharmaceuticals required a modification of the scintigraphic equipment. Thus in the 60's the commercial scintigraph was adjusted for Sr-85 use by strengthening the collimator with lead. In collaboration with the Institute Jožef Stefan own whole-body scanner was developed and constructed by a local Railway workshop; the scanner proved very handy for fast bone imaging with F-18, which was among the most pretentious examinations performed.

The importance of the described device for skeletal scintigraphy could not be diminished even by the use of Tc-99m labelled polyphosphates an gamma camera purchased in 1974. The whole-body scintiscan had been used in patients with radioactive Fluor-18 applications all until the middle of the 80's.

The third device which was developed in collaboration with the Institute Jožef Stefan and the colleagues from Celje was the already mentioned renograph.

Homemade Computer Programs:

In the same way as the staff of the Unit headed by M. Erjavec developed their own measuring instruments, they also produced their own computer equipment. The beginnings reach back into late 60's when the first original digital amplifier for contrast scintigraphy was developed. Around the year 1968, with first computers coming into use, they developed a system of digital recording of information on a perforated band, which lead to the first system for computer processing and presentation of images. The top achievement was certainly their own program for hidden-lines isometric graphic presentation which was considered an advance even by the most developed centers in the world.

In 1972 the Unit obtained its own computer HP 2100 in virgin configuration. By the help of experts Jožef Stefan Institute, it was linked into a computer net connecting all the measuring devices in the laboratory. In 1974, the computer system was enhanced by inclusion of a gamma camera Nuclear Chicago Pho Gamma 4.

By breakdown of the computer in 1978, the programming work had been completely stagnating until 1984 when the Institute of Oncology obtained another gamma camera, produced by General Electrics, which comprised a computer Star and ready made programs that only needed to be adjusted to the specific needs of UNM

Radiopharmacy:

Around the year 1970, radiopharmacy mainly referred to in-house labelling of different ra-

diopharmaceuticals, in the beginning by means of Iodine-131 and later on with In-113. A major effort was devoted to the labelling of macroparticles for lung scintigraphy, and of microspheres for lymphography and scintigraphically guided intraarterial chemotherapy which has become widely recognized only 15 years later. All attempt to use intravasal applications of radionuclides with therapeutic intent have failed. Anyway, the therapeutic applications of radionuclides represented only 1 % of the Unit's routine.

Therapy:

Up to 1970, patients with sealed and open radioactive sources had been treated in this Department, whereas after the establishment of Brachyradiotherapy Department in that year, only open sources were applied in UNM.

After the introduction of intracavitary therapy with radioactive coloid gold 185, and metabolic therapy of thyroid tumors with Iodine 131 in the 50's, in the next decade the treatment for painful bone metastases by means of radioactive Phosphorus 32 and Strontium 89 came into use. As the therapeutic radiolymphography with iodised oils appeared quite promising, in 1967 own production of this radiopharmaceutical was started. The method, however, proved clinically irrelevant and was therefore abandoned. In the 80's, the above applications were enhanced by experimental use of therapeutic doses of 131-I-metaiodobenzylguanidine (131-I-MIGB).

In 1984, the team of 17 workers of DNM, headed by M. Erjavec, performed 9930 *in vivo* investigations and applied therapeutic doses of pharmaceuticals in 60 patients.[11]

1973 – Maribor: General Hospital Maribor, Departments of Internal Medicine, Nuclear Medicine

In the appointed year, a Laboratory for Nuclear Medicine was allocated its room of 180 m^2 on the first floor of the building intended for these purposes. Nuclear Medicine in Maribor was started by R. Turk and five of his coworkers. The initial equipment comprised a scintiscanner Nuclear Chicago, a renaltron Nuclear Chicago, a measuring device for Iodine uptake in the thyroid, and an automatic sample measuring device for *in vitro* investigations.

In 1984, the staff of 14 workers employed in the Dept. of Nuclear Medicine, headed by R. Turk and J. Šubic, performed 9731 *in vivo* examinations, and applied therapeutic doses of radiopharmaceuticals to 36 patients; they also carried out 16,978 *in vitro* investigations.[12]

1974 – Koper: Health Center Koper, General Hospital Izola, Unit for Nuclear Medicine Ankaran

This Unit started to work in July 1974. For the needs of NM service, 104 m^2 of place occupying 8 rooms were allocated in the Department of Internal Medicine of the hospital in Ankaran. This relatively small surface had to accommodate a common work room, hot laboratory, 2 measurement rooms for *in vivo* examinations, a room for application of radiopharmaceuticals, radiochemistry, waiting-room and an outpatient office with administration.

In the beginning, the staff consisted of a doctor – A. Malej, and an X-ray technician – M. Ogris with four technical coworkers; weekly consultancies were attended by the specialists M. Erjavec from Ljubljana, and F. Fazarinc from Celje. The Laboratory covered for the needs of the region including Koper, Izola, Piran, Sežana, partly Pivka and Postojna, and the Croatian part of Istria incl. Buje.

In 1984 the unit employed 8 workers headed by A. Malej, who performed 3110 *in vivo* and 6159 *in vitro* examinations, as well as 8 applications of therapeutic doses of radioiodine.[13]

1974 – Šempeter near Gorica: General Hospital, Department for Endocrinologic Diseases and Nuclear Medicine

The initiator of nuclear medicine in this part of Slovenia was B. Gornjak. In the school year 1973–74 he successfully completed the first postgraduate study of nuclear medicine in Ljubljana. Also both technicians underwent a 6 month training at the Institute of Nuclear Medicine in Ljubljana.

The 28th of October 1974 denotes the beginning of regular work in the Unit. On that day, the first renography was performed in a patient with suspected urolithiasis. When the 4-channel kinetograph (developed by Jožef Stefan Institute) produced its first renographic curve, the scarce staff of the unit including its head felt very proud of the achievement.[14]

The unit soon obtained additional equipment, i.e. semiautomatic sample measuring device AMES-Gammacord II, and in 1975 also a scintiscanner Nuclear Chicago. The number of investigations performed rapidly increased, and also the circle of users got wider. Apart from renographies, the Laboratory also performed scintiscans of the thyroid, kidneys and liver.

In 1984, the Department with the staff of 6 workers, headed by J. Burnik, performed 2042 *in vivo* and 3521 *in vitro* examinations, and 11 applications of therapeutic doses of radioiodine.[14]

Conclusion

The beginnings of seven different units of nuclear medicine in the hospitals of Slovenia with about 2 million population are presented. Each of these units was something special.

The most prominent advance was made by the Clinic in Ljubljana. Thanks to the endeavours of the pioneer of Slovenian nuclear medicine B. Varl, a simple laboratory at the Clinic of Internal Medicine has developed into a University Clinic for Nuclear Medicine with four departments: for *in vivo* and *in vitro* diagnostics and therapy, with a hospital ward and an outpatient department. This institution maintains the highest professional level of nuclear medicine in Slovenia, and represents a teaching basis for postgraduate studies in the appointed field of medicine. It also provides residency program for physicians – future specialists in nuclear medicine, and is the seat of the Section for Nuclear Medicine of the Slovenian Medical Society.

Opening of all seven Slovenian nuclear medicine units was promoted by rapid development; the 70's were the decade of great advances in nuclear medicine in the World as well as in Slovenia. The rapid development of this branch of medicine round the year 1970 could be attributed to the introduction of gamma camera, computer, Tc-generator, and radioimmune assays. Seemingly uncontrollable boom of nuclear medicine of the 70's by the end of the decade had to give way to new achievements in rentgenology and biochemistry. Hospitals tended to give preference to ultrasonographic and CT equipment over gamma cameras, whereas in *in vitro* diagnostics radioimmunoassays were replaced by enzyme and immunofluorescent tests which are devoid of radioactive materials. Thus, in the 80's, the new techniques developed in allied medical branches contributed to the advances in radiology, ultrasonography and biochemistry.

The expansion of nuclear medicine from Ljubljana into peripheral hospitals goes hand in hand with the period of rapid development of this new medical branch. With the establishing of seven Departments of nuclear medicine by 1974 the needs of Slovenia were fully covered. Further development was centred on the endeavours for obtaining most essential pieces of new equipment, improvement of room facilities, introducing of new investigation, establishing and maintenance of international collaboration etc.

The frequency of investigations reached its peak by the end of 70's, and annual number of investigations performed in the 80's remained basically unchanged. A review of the activity in 1984 for the whole Slovenia with the population of approx. 2,000,000, gives the following figures: 44,215 *in vivo* and 185,175 *in vitro* investigations, and 504 applications of therapeutic doses of radiopharmaceuticals were performed. By the 80's, nuclear medicine has finally reached its present stage when the quantitative development has been replaced by a qualitative one.

peared in 6.6%, whereas fistulas and malabsorption syndrome were not noted.

2) *Study No. 22844:*

This was a randomized study aimed to establish the effectiveness of postoperative irradiation of gliomas of low-grade malignany according to two different dose regimens.

The study was completed by October 1991 and comprised 397 patients. The preliminary analyses did not establish any difference in the survival of patients with high–dose and those with low-dose irradiation.

3) *Study No. 22851:*

The subject of this randomised study was accelerated fractionated radiotherapy in advanced head and neck carcinomas.

In a previously performed study classical and hyperfractionated radiation regimen with 70 fractions of 115 cGy were compared. A statistically significantly better local tumor control was achieved in patients with fractionated radiation regimen, whereas the rate of late side effects was equal in both groups despite the higher dose received during hyperfractionated irradiation.

Of 424 patients 157 have already died, 106 of cancer, and 10 of radiotherapy-related complications; 8 of these patients belonged to the hyperfractionation group.

Acute reactions grade 3 and 4 were noted in 60%, their rate in conventional vs hyperfractionated regimen being 40:60 respectively. Late side effects were equal in both groups. Neurologic complications that occurred in 1 patient required the dose to the spinal cord to be reduced to 36 Gy. The dose also had to be reduced because of another 3 (of approx. 2000) patients receiving accelerated hyperfractionated irradiation (CHART regimen) owing to treatment related spinal cord damage.

Radiobiologic investigations performed within the frame of this study have shown that there are probably two periods for DNA repair, the fast and the slow one, the latter probably lasting over 24 hours.

Preliminary results of the investigations of cell kinetics by means of IUDR labelling and flow cytometry indicate that fractionated irradiation is significantly more successful in tumors with T-potential less than 4 days. The study was carried out on 100 patients, in collaboration with 22 centers.

4) *Study No. 22861:*

The randomized (phase II) study of anal cancer treatment using a combination of radio- and chemotherapy, or radiotherapy alone included 86 patients from 27 different centers.

Complete response (CR) was achieved in 65% in the first arm, and in 20% in the second arm of investigation.

5) *Study No. 22863:*

Treatment for prostatic carcinoma which is associated with a hihg risk of dissemination is being studied; treatment with irradiation alone is compared with a combination of irradiation and hormonal therapy.

There have been 216 patients from 19 institutions included in the study.

Zoladex medication is maintained throughout the duration of 3 years in form of yearly depo applications. The treatment is associated with few acute side effects, whereas of the latter ones the potency was found to have reestablished after the cessation of therapy.

6) *Study 22881/10882*

This study is concerned with conservative therapy of breast cancer (phase III), and the evaluation of the relevance of booster dose in radiotherapy.

So far, 1934 patients from 26 institutions have been included.

Owing to the fact that 93.7% of patients had complete resection, only few patients were included in the second arm of the study.

Before joininig the study, all centers had to describe their standard systemic therapy which was not to be changed throughout the study period.

The study program includes also irradiation quality control. In all centers preliminary analyses were carried out in the first 10 treated patients; based on the recommendations of

physicists irradiation technique was improved, upon which the last ten included patients were evaluated in all centers.

The dose in point A, which is defined as an intersection of central opposite field beams, in over 97% reaches the exact value of 50 Gy. Also the dose in point B, which is defined in the site of excised tumor, is frequently found to be 50 Gy; this, however, does not seem very reliable and requires further confirmation.

When comparing boost volumes, a considerable range of values (max. approximately 1000 ccm) was established, though there was no correlation between the boost volume and dose.

7) *Study 22911*

Postoperative irradiation in prostatic carcinoma stage pT3 is studied.

The probability of relapse after surgery alone is 20–40%, whereas with additional postoperative irradiation this rate has been reduced to 10%. It is expected that a difference in the range of 75–90% would be established between both investigation arms after 5-year study period; in order to prove this, at least 105 new patients will have to be entered into the study. However, since many patients do not meet the entry requirements, the final number of patients required approaches 300.

8) *Study 10853*

The investigation is centred on ductal breast carcinoma *in situ*.

So far 425 patients have been included. As many as 7 centers have contributed only a single case each, whereas 8 other centers participated with 2–3 cases each.

Studies to be commenced

1) *Study 22921*

Therapy for rectal carcinoma stage T3, T4 will be evaluated. Staging will be preferably supported by the use of endorectal ultrasonography.

Irradiation dose is 45 Gy per 5 weeks, delivered in 1.8 Gy fractions.

The initial randomization will be done preoperatively, when the patients will be distributed into two investigation arms, i.e. into a group treated by irradiation and a group receiving both irradiation and chemotherapy (5-FU and Leukovorin, 350 mg/m^2 through 3 days). The patients will be again randomized postoperatively: one study arm will remain without any additional treatment whereas the other group will receive 4 cycles of adjuvant chemotherapy.

The criteria for exclusion before the second randomization are as follows:

- incomplete resection
- metastases
- performance status (WHO) >2
- treatment-related gastrointestinal complications grade 3
- hematologic toxicity grade 2
- patient's refusal of therapy

The study proposal is supported by the results of a pilot experiment which has confirmed that a dose of 350 mg/m^2 5-FU is still tolerable whereas a dose of 420 mg is not. The main difficulty related to chemotherapy is diarrhea.

This trial has already been approved in France.

2) *Study 22922*

This is a randomised study on the irradiation of the internal mammary chain lymph nodes after surgery for breast carcinoma stage I–III.

The proposal has been resubmitted for consideration by the Protocol Review Committee (PRC).

New study proposals

1) *Study on ARCON*

The use of ARCON (Accelerated Radiotherapy with CarbOxen and Nicotinamide) seems sensible since the inhalation of carbogen reduces chronic hypoxia in the tumor while nicotinamide influences acute hypoxia caused by the cyclic closing of the tumor vessels. Experiments on mice in Gray's laboratory have shown that up to 1.9-times enhanced effects of irradiation can be expected by this method.

According to the clinical data obtained so far, the dose 6 g of nicotinamide per day is quite safe and free of any adverse side effects.

The following treatment regimen was suggested for bronchial carcinoma: irradiation twice daily with 1.5 Gy fractions and a free interval of 8 hours up to the cumulative dose of 60 Gy in 40 fractions, delivered in 20 days.

Accelerated irradiation for head and neck sites should be basically the same as in the study 22851.

2) A randomised study on *postoperative treatment for ovarian carcinoma* stage I and II by irradiation or chemotherapy is being prepared.

After surgery, the patients will be randomized into two study arms. The first groupe will receive TAI (total abdominal irradiation) as adjuvant therapy in the following schedule: dose 25 Gy, fractions 1.25 Gy/day, without liver shielding though with protection of the kidneys, followed by irradiation of the pelvis according to the previously described regimen.

The second group will receive postoperative chemotherapy with Platinol, 75 mg/m^2 every 3 weeks, 4–6 cycles.

The treatment is commenced within 6 weeks following surgery.

Seventeen institutions have already registered their participation in the study, and the cancer centers from Ljubljana and Zagreb are also going to take part in it.

3) Study proposal for *postoperative irradiation of head and neck carcinomas* (oral cavity, oropharynx, hypopharynx, paranasal sinuses).

After surgery, the patients would be distributed into two groups, i.e. into a high-risk and low-risk group. The criteria for the "high–risk" classification are as follows:

- T3, T4, N2–3
- incomplete resection
- carcinoma invasion through the lymph node sapsule.

Suggested therapy:

a) for low-risk group: the 1st study arm: 54 Gy in 5.5 weeks

the 2nd study arm: 66 Gy in 6.5 weeks

b) for high-risk group: 66 Gy in both investigation arms, and afterwards randomization into the 1st arm receiving no additional therapy, and the 2nd arm receiving chemotherapy with Platinol 70 mg/m^2 week, 6 cycles.

It was pointed out in the discussion that such a chemotherapy regimen can be very aggressive, but dr. H. Bartelink explained that the feasibility of the suggested therapy was confirmed by the results of a pilot study.

New proposals to be discussed

1) Proposal of a study for the evaluation of *stereotactic method for irradiation of brain metastases.*

Patients with 1–3 brain metastases (carcinoma or sarcoma) will be randomized into two study arms: one receiving classical irradiation (10×300 cGy), and the other with stereotactic approach where a single fraction of 20 Gy will be used with isodose of 80 % covering the whole metastasis. The final proposal will be prepared by the Radiosurgery Committee till the next meeting.

2) Study proposal on the role of *irradiation in the treatment of nonsmall cell bronchus carcinoma* (NSCBC).

The incidence of lung cancer takes the first place in Slovenia as well as in Europe, and represents about 25 % of all cancer-related deaths. The prognosis in patients with bronchus cancer has not improved significantly during the last 30 years, and less than 10 % of patients are expected to survive 5 years form diagnosis.

Small cell bronchus carcinoma represents approximately 20 % of all bronchus carcinomas. With respect to its early metastasizing and sensitivity to a number of chemotherapeutic agents, chemotherapy is considered the treatment of choice.

On the other hand, NSCBS is known to be rather chemoresistant. Therefore, radical resection offers the best chances for cure. In localized tumors stage T1-2, N0, 5-year survival is more than 50 %.

Of all newly detected patients with NSCBC, 50 % are found inoperable already on the first clinical examination, additional 20 % on bronchoscopy, and 10 % more on explorative thoracotomy. Of the remaining 20 % patients, only 30 % of that are alive 5 years after surgery.

In patients with localized though technically inoperable NSCBC, who have been treated by radiotherapy, 5-year survival is observed in 20–50 %; these are generally the patients with stage T-2 and NO, who would have been operated on, had it not been for their old age, other diseases etc. which overrule the possibility of surgery. They were irradiated with a dose up to 50–70 Gy.

A majority of patients with NSCBC present with advanced disease; their median survival is 8–12 months, and 5-year survival less tha 10 %. Treatment in these patients is of palliative nature only, and has but a negligible effect on their survival.

In Europe as well as in the United States of America, the role of irradiation of these patients depends more or less on individual centers, and even more frequently on individual opinion of the therapist. A number of recent reviews have pointed out very differing approach irradiation so with respect to the doses and fractions used, as well as with respect to the prognosis. There is no uniform opinion on when radiotherapy should be regarded as palliative and when as curative. Also in palliative irradiation the doses are greatly differing, and so are also the indications for therapy. These range from the opinion that radiation is performed merely with a palliative intent to alleviate symptoms such as pain, bleeding and respiratory distress, to the belief that irradiation should be used as a preventive measure.

In a previous study by Bleehan, two irradiation regimens were compared in a randomized group of patients. The first group was irradiated with the dose of 17 Gy in two fractions, and with 1 week interval, whereas the second group received 30 Gy in 10 fractions and 2 week interval. There was no difference in the results with regard to patients survival (median 6 months), the improvement of symptoms and the duration of that improvement.

According to a new proposal for study of the role of irradiation in the treatment of non-small cell bronchus carcinoma, the patients are distribute into 3 groups:

A – patients with favourable prognosis, presumably curable by high-dose radiotherapy;

B – patients with no practical chance of cure, but in whom the treatment for local tumor control is expected to result in a prolonged survival and an improved quality of life;

C – patients with poor prognosis and expected survival less than 6 months; a majority of them suffer from disease-related simptoms, and therefore the therapy is directed into alleviating difficulties.

Suggested therapy:

Group A:	not eligible for this study;	
Group B:	1st RT:	30 Gy/10 fractions
		60-65 Gy/30–33 fractions
	2nd RT:	30 Gy/10 fractions
		10 Gy/1 fraction
Group C:	3rd RT:	30 Gy/10 fractions
		10 Gy/1 fraction

The first group was aimed to established the possibility of cure by means of high-dose iradiation, or to answer the question whether such a regimen enables a better local tumor control.

In the second group, a possible advantage of fractionated regimen over single-fraction irradiation, as well as it influence on survival and alleviation of symptoms should be established.

The third group was designed with the aim to establish the lowest possible dose and the simplest irradiation regimen able to result in alleviation or control of symptoms.

Owing to a large number of patients with NSCBC in Europe, we can expect the study to be completed very soon. The results obtained should have a significant influence on the survival of these patients which represent a great burden for all radiotherapy centers.

Boris Jančar, MD
Institute of Oncolgy, Ljubljana

Radiol Oncol 1992; 26: 338-9.

Course on scientific and medical illustrations

September 2–4, 1992, Krems/D, Austria

IPOKRaTES (International Postgraduate Organisation for Knowledgetransfer, Research and Teaching Excellent Students) is an international organization which has been established with the aim to promote a higher level of research projects and their presentation. Within the scope of its activities it organizes various courses intended for both the research workers as well as for those who are in one way or the other directly involved in the processing of their investigation results (e. g. reviewers, editors etc). One such course dedicated to the relevance and techniques of scientific and medical illustration was held in September last year in Krems, Austria.

It is an indisputable fact that an illustration offers more direct and easy-to-understand information than a written or spoken text, and as such it facilitates the exchange of scientific information for both the conveyer and the recipient. It represents an explanation, support and confirmation of the reported scientific result in one. Illustrations differ as to their purpose, and can be categorized into three main groups, i. e. 1) for written/printed communications, 2) slide projection and 3) for poster presentation. Whereas the first may comprise a relatively extensive and complex information, those that serve the latter two purposes should be as brief as possible, containing only the most essential key data. **Drawings** often have the advantage over photographs by offering the possibility of simplification, marcation of details, and not requiring a background. **Photographs** should be of adequate contrast, centred on the presentation of a detail which should be positioned centrally. In sonograms, a conic sector of the ultrasonographic image without lateral background would generally be sufficient.

Today, the design of **tables** is almost equal in all publications. A few horizontal lines separating the title, table head, totals and foot-notes are acceptable, whereas any vertical lines between columns are considered redundant and cannot be seen frequently. The size and contents of the table should be such as to enable the reader to grasp the information without much effort and laborous reading of details, which particularly refers to the units and terminology used.

By means of **graphs** we can present numeric data in form of columns, curves of points in order to illustrate e. g. an increase or decrease of values, differences between them, as well as their correalation and trends. Columns being generally vertical, the abscissa (x) in graphs is mostly considered unnecessary. It is important that the value scale on abscissa (x) and ordinate (y) should start with zero (0) value. In the opposite case, the distance should be clearly marked with a set-off or a disruption on both the curve and the axis. Any curve-related marks should best be placed as close to the curve as possible, rather then being written dissociated just anywhere in the graph or even below it. More important curves can be highlighted, whereas those presenting different values, though of the same rank of importance, should be marked so as to remain within the same rank. An open graph conveys the message more clearly than a closed one (in form of a rectangle or square). When submitting graphic materials (graphs and photographs) for final editing, the size of publication and the width of text columns

should be taken into account, since any reducing may result in poor legibility of the figures.

General guidelines for **poster** preparation are usually given by the organizer of the event where the poster is to be presented, but nevertheless it should be carefully designed. Considering the short time when authors are available to explain their works, a large number of paricipants and posters, and frequently inadequate exhibition place, a poster must be as simple as possible, centred on few basic points of the investigation. Should author wish to give more details, he is advised to do so in a written synopsis that can be distributed to interested participants.

The course held by Mrs. M. H. Briscoe dealt with a number of problems related to scientific illustration, all from the initial idea to its final materialisation. It was supported by practical use of computer for processing of graphs, as well as by the book "A Researcher's Guide to Scientific and Medical Illustrations".

Rather than passively attending a cycle of lectures *ex catedra,* the participants were expected to take active part by asking questions and suggesting possible solutions to the posed problems. The most advanced possibilities of graphic presentation of scientific work were shown and discussed. These are governed by own strictly defined regulations, though it may sometimes appear that a figure was created *ad hoc,* self-evidently depending on the author's endeavours. A valuable research work, impecable as its performance might have been, means nothing but a waste of time and money, had it not been properly presented.

Tomaž Benulič, MD, MSc
Institute of Oncology, Ljubljana

Notices

Notices submitted for publication should contain a mailing address and phone number of a contact person or department.

Genito-urinary tract tumours

The ESO training course for Central and Eastern Europe will be held in Grossenzersdorf, Vienna, Austria, *July 19–21, 1993.*

Contact European School of Oncology – Vienna Office, Arztekammer Fuer Wien, Weihburggasse 10–12, 1010 Vienna, Austria; or call + 43 222 51 501 280. Fax: + 43 222 51 501 240.

Lung cancer

The ESO training course for Central and Eastern Europe will be offered in Grossenzersdorf, Vienna, Austria, *September, 1993.*

Contact European School of Oncology – Vienna Office, Arztekammer Fuer Wien, Weihburggasse 10–12, 1010 Vienna, Austria; or call + 43 222 51 501 280. Fax: + 43 222 51 501 240.

Tumour imaging

The ESO seminar will take place in Venice, Italy, *September 8–10, 1993.*

Contact European School of Oncology, Via Venezian, 18 20133 Milan, Italy; or call + 39 2 70635923 or 2364283. Fax: + 39 2 2664662.

Medical physics

Medical Physics 93 & The 9th Spanish medical physics congress, including a joint EFOMP/ESTRO session on portal imaging, will be held in Puerto de la Cruz, Tenerife, Spain, *September 22–24, 1993.*

Contact the ESTRO Secretariat – University Hospital St. Rafael, Radiotherapy Department, Capucijnenvoer 35, 3000 Leuven, Belgium; or call + 32 16 33-64-13. Fax: + 32 16 33 64 28.

Head and neck tumours

The ESO training course for Central and Eastern Europe will be offered in Grossenzersdorf, Vienna, Austria, *September 30 – October 2, 1993.*

Contact European School of Oncology – Vienna Office, Arztekammer Fuer Wien, Weihburggasse 10–12, 1010 Vienna, Austria; or call + 43 222 51 501 280. Fax: + 43 222 51 501 240.

Oncology

The ESO training course for Central and Eastern Europe, titled "Good clinical practice", will take place in Grossenzersdorf, Vienna, Austria, *September, 1993.*

Contact European School of Oncology – Vienna Office, Arztekammer Fuer Wien, Weihburggasse 10–12, 1010 Vienna, Austria; or cal + 43 222 51 501 280. Fax: + 43 222 51 501 240.

Oesophageal mucosa

The 4th International Polydisciplinary Congress of O.E.S.O. (International Organization for Statistical Studies on Diseases of the Oesophagus) will be held in Paris, France, *September 1–4, 1993.*

Contact Michele Liegeon, O.E.S.O.; 2, Boulevard du Montparnasse, 75015 Paris, France; or call + 33 1 45 66 91 15. Fax: + 33 1 45 66 50 72.

Radiation physics

The ESTRO teaching course "Radiation Physics for Clinical Radiotherapy", will be held in Leuven, Belgium, *September 5–9, 1993.*

Contact the ESTRO Secretariat – University Hospital St. Rafael, Radiotherapy Department, Capucijnenvoer 35, 3000 Leuven, Belgium; or call + 32 16 33-64-13. Fax. + 32 16 33 64 28.

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Editors greatly appreciate the work of the reviewers which significantly contributed to the improved quality of our journal.

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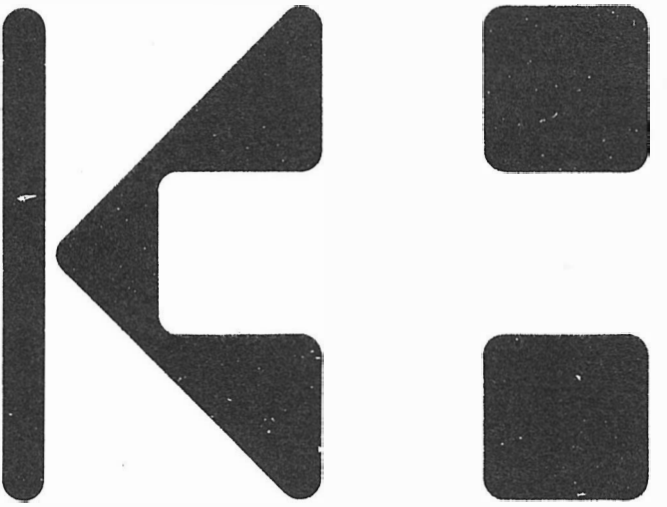

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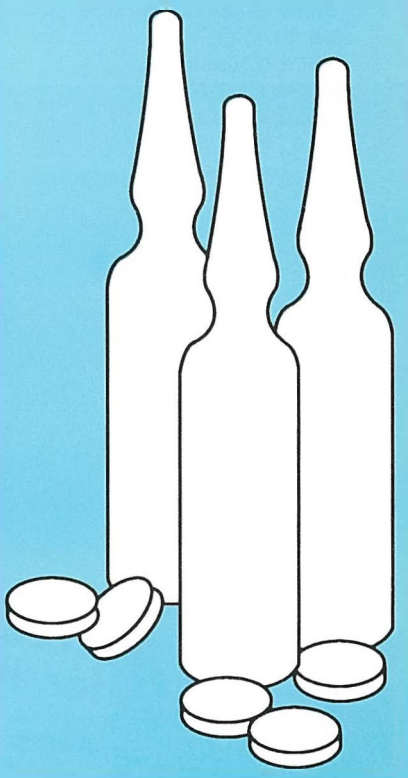

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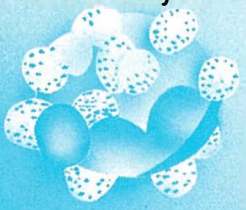

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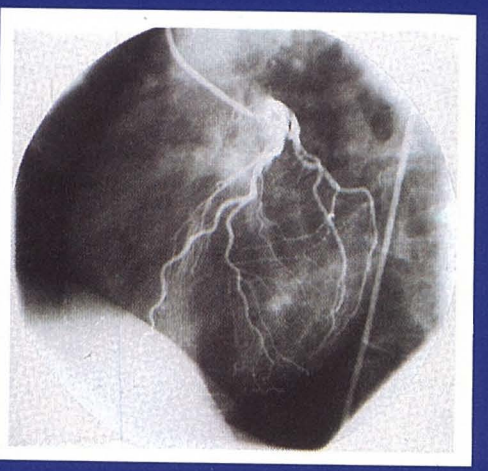

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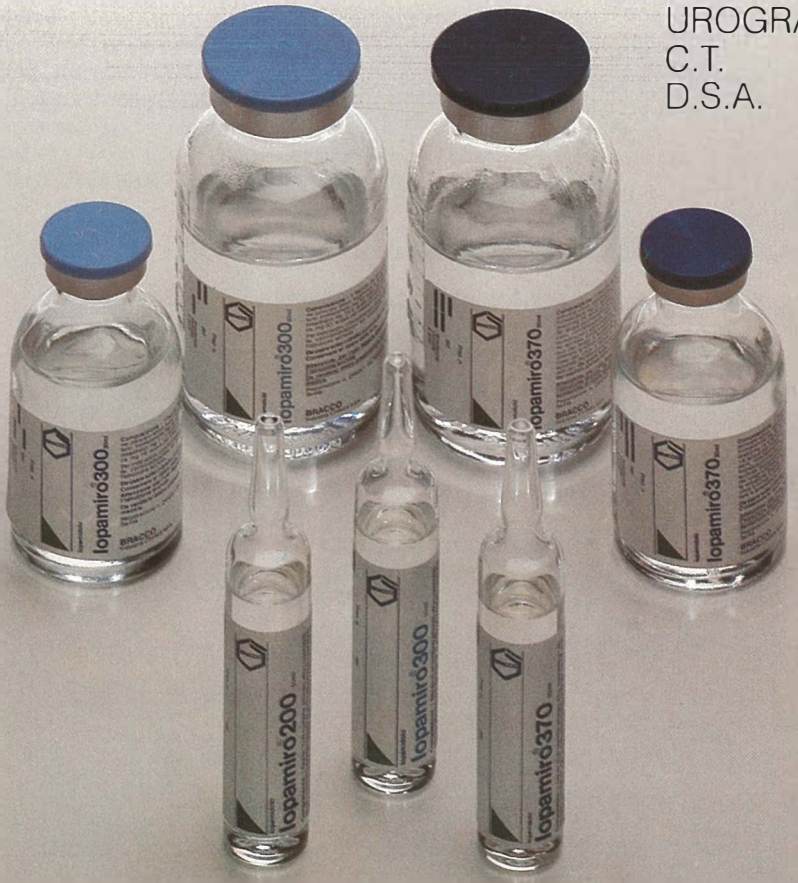

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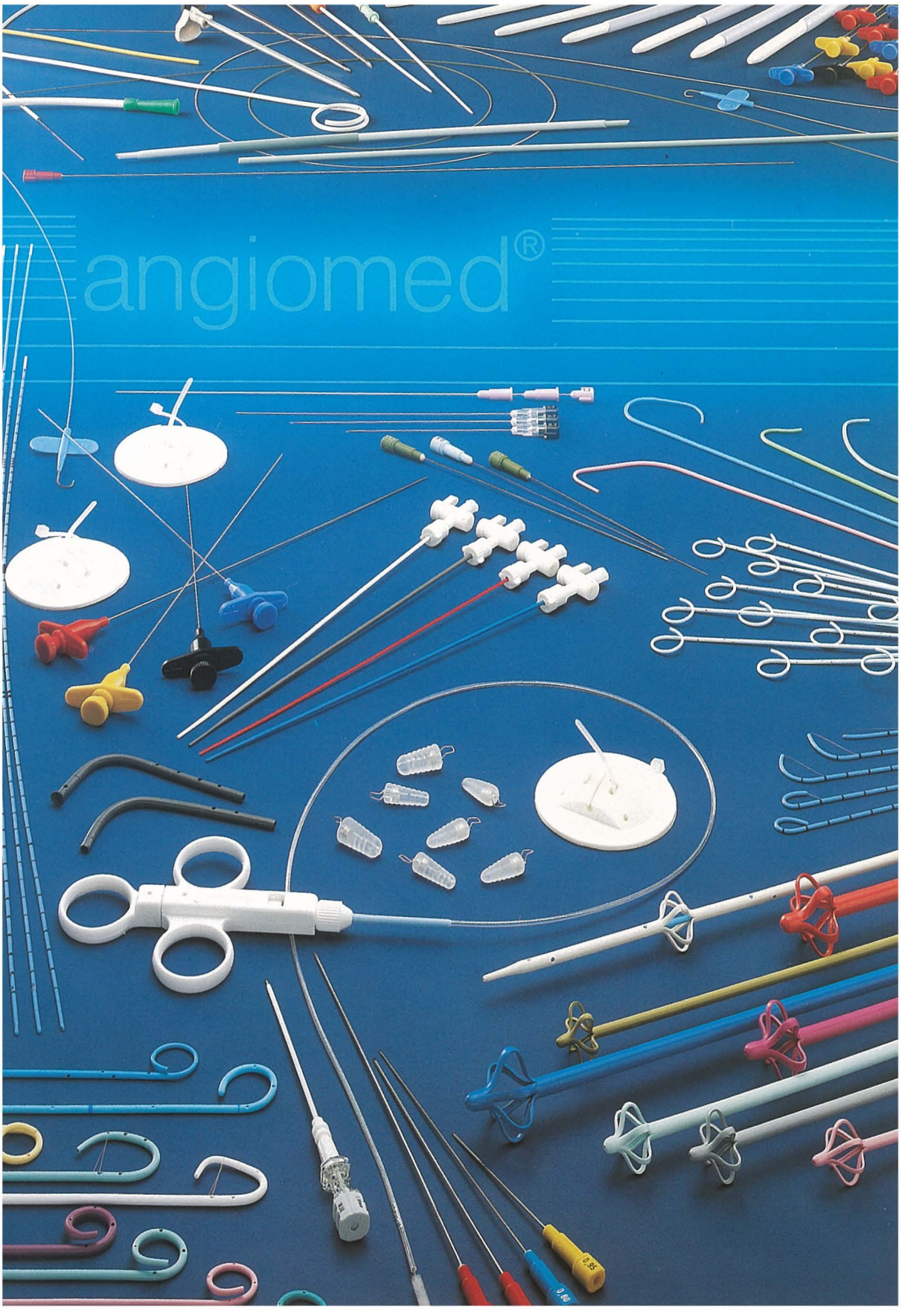
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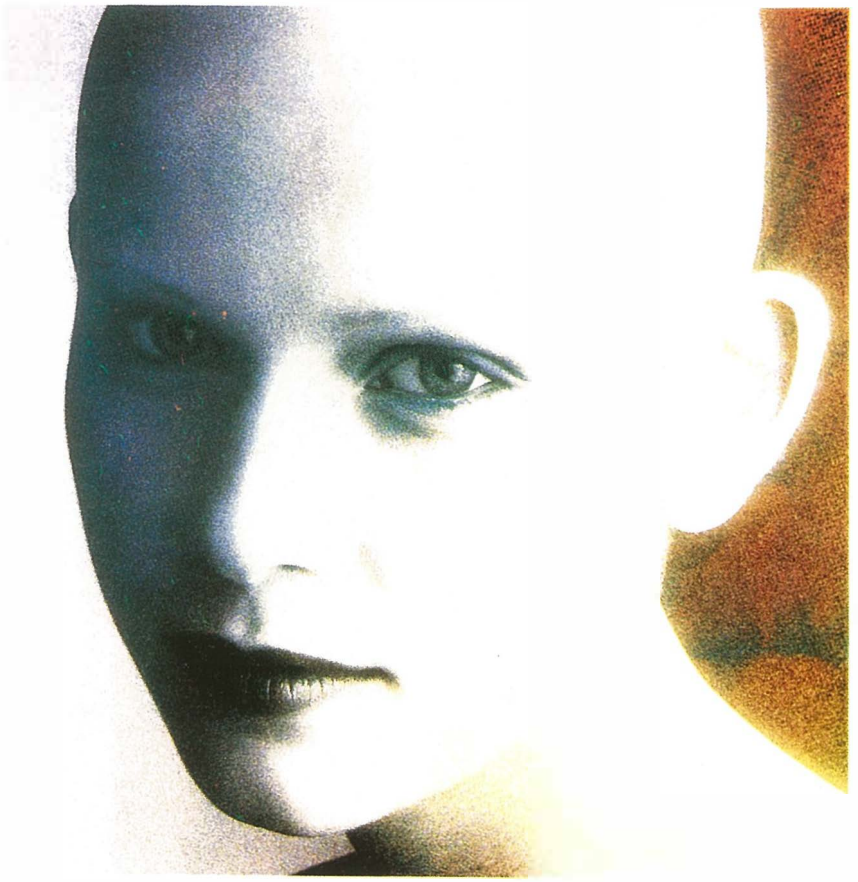

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Odrasli: Visokoemetogena kemoterapija: Doza po 8 mg s počasno iv. injekcijo neposredno pred kemoterapijo in še dve iv. dozi po 8 mg v presledku po dve do štiri ure, ali nepretrgana infuzija 1 mg/uro do 24 ur. Za zaščito pred zakasnelim bruhanjem, po preteku prvih 24 ur, nadaljujemo z oralnim dajanjem Zofrana po 8 mg 2-krat dnevno do 5 dni po ciklusu zdravljenja. Emetogena kemoterapija in radioterapija: Zofran po 8 mg dajemo v počasni iv. injekciji neposredno pred ciklusom zdravljenja ali oralno eno do dve uri pred ciklusom in nadaljujemo z oralnim dajanjem po 8 mg vsakih dvanajst ur. Za zaščito pred zakasnelim bruhanjem, po preteku prvih 24 ur, nadaljujemo z oralnim dajanjem Zofrana po 8 mg 2-krat dnevno do 5 dni po ciklusu zdravljenja.
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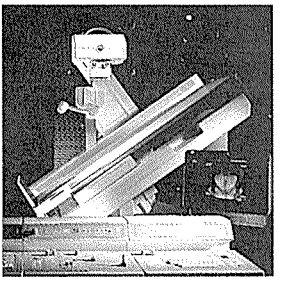

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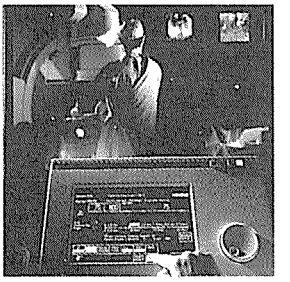

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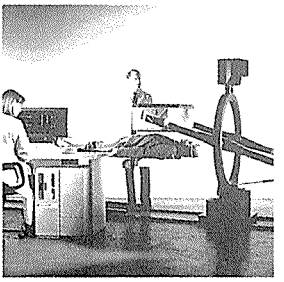

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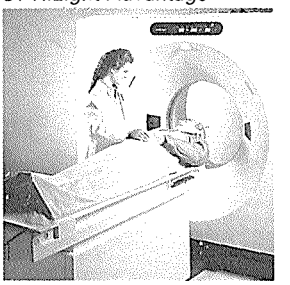

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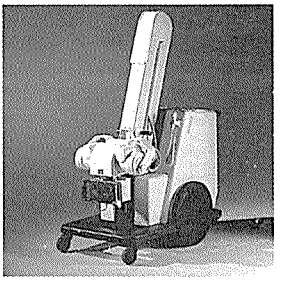

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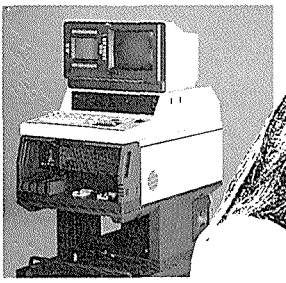

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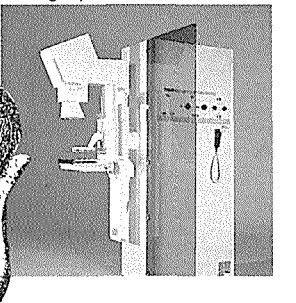

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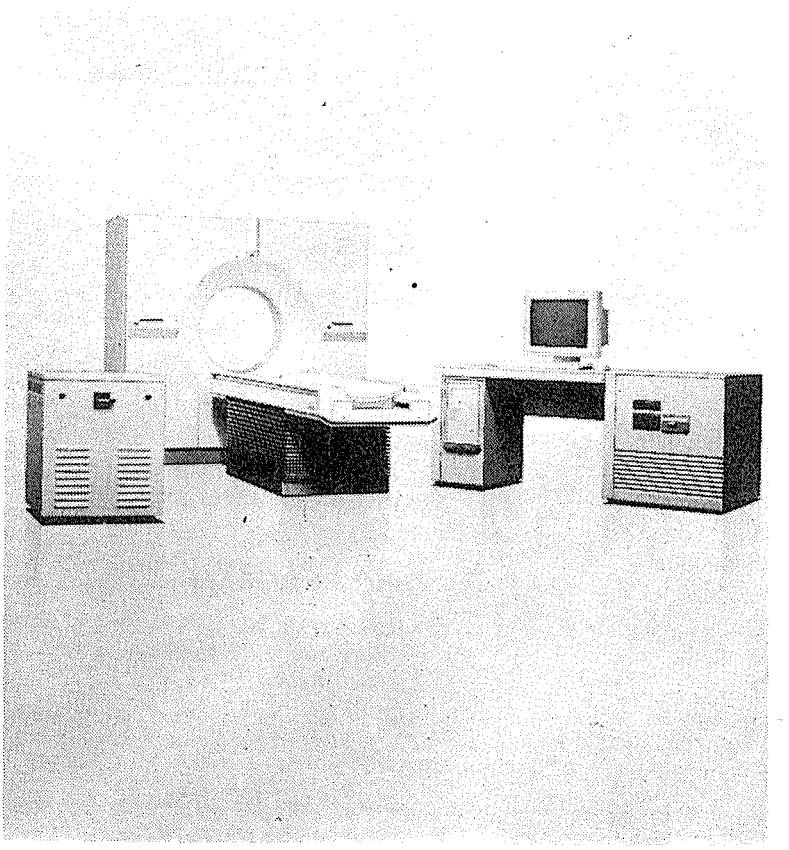

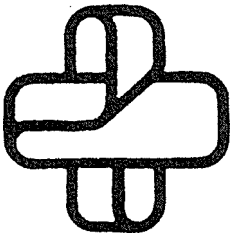

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