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Radiol Iugosl October – December 1991; 25:283-376

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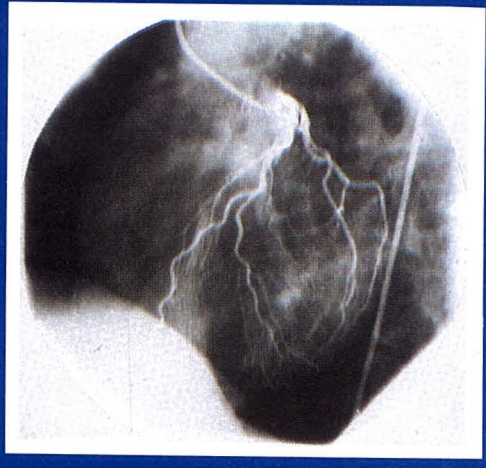

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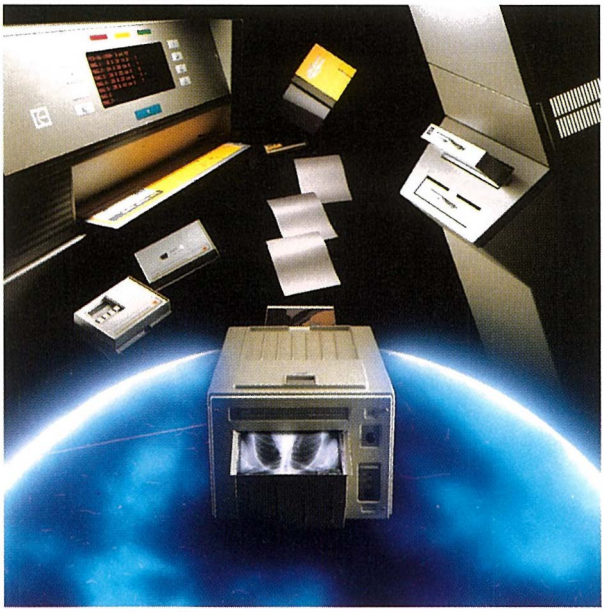

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RADIOLOGIA IUGOSLAVICA

ANNO 25 1991 FASC.4

On the Publication of the 25th Volume

As the present No.4/91 of RADIOLOGIA IUGOSLAVICA actually represents the 25th volume of our journal, and thus symbolises its successful continuation, it seems right that we say a few words about its beginnings and development till now.

The start of our activity reaches back to the year 1964. At that time, on the occasion of the IVth Yugoslav Congress of Radiology, a decision on the foundation of a radiological journal was taken at the initiative of Prof. Dr. Božena Ravnihar. From the very beginning till now, the seat, i.e. editorial office of this newly established journal has been situated at the Institute of Oncology in Ljubljana. The first and many following issues were edited and prepared by Prof. Dr. Stojan Plesničar, in collaboration with one of the pioneering editors and coworkers of our journal, Prof. Dr. Ivo Obrez.

Thus, after several years, RADIOLOGIA IUGOSLAVICA successfully filled the gap left behind after discontinuation of »Radiološki glasnik« that had been appearing in the period between 1935-1940 in Zagreb. Let us hope that the recent war entailed by the disintegration processes in Yugoslavia will not in a similar way interfere with the publication of our journal.

In the past 25 years there were over 12000 pages of scientific and professional papers as well as other contributions pertinent to the fields of x-ray diagnostics, nuclear medicine, oncology, radiobiology, radiophysics, radiation protection and allied subjects published by our journal. By the development of new, specially technical, subfields in medicine, contributions covering the topics of ultrasonography, computed tomography and magnetic resonance etc. have been gradually included in our journal.

From the very beginning the journal has been appearing regularly on the quarterly basis; apart from these regular numbers, there were also occasional supplements published which were dedicated to particular topics of medicine.

Our tendency to favour English over national languages was based on the idea that in this way the journal could surpass the borders of a national publication and enable a more efficient flow of scientific information.

Among the authors are many renowned national and international professionals and scientists, as well as numerous promising young research workers. Thus our journal has been playing an important role in the professional education in the field of scientific publishing, and for this important mission deservedly received a number of awards from Yugoslav federal and national institutions.

Without exaggeration we can say that, due to its permanent development in the design and context, our journal is abreast of other similar publications abroad.

On the occasion of our 25th anniversary, the editorial board has decided to publish a book entitled **»Advances in Radiology and Oncology«.** The publication is being prepared in collaboration with many prominent national and foreign authors, and will comprise a number of outstanding original scientific papers and review articles in the fields covered by our journal. It is hoped that the book will be well accepted by the worldwide scientific community. On the other hand, the experience gained through its editing and publication will prove invaluable for our future development and will influence the editorial board's policy in preparing further regular numbers of the journal.

On this occasion our due thanks should be given to the authors and coworkers whose collaboration enabled the continuation and development of our activity despite the present difficult situation that we face nowadays.

If our mutual efforts and dedication have in any way contributed to the promotion of medical science and related to it improved quality of patients' life, this would be the best reward for the staff as well as for all the coworkers of our journal.

Tomaž Benulič, MD,
Editor-in-Chief

UNIVERSITY OF RIJEKA, MEDICAL FACULTY, DEPARTMENT OF ANATOMY
CLINICAL HOSPITAL CENTER RIJEKA, DEPARTMENT OF RADIOLOGY

RADIOLOGICAL ANATOMY OF THE STOMACH AND DUODENUM FOLLOWING VAGOTOMY AND PYLOROPLASTY

Dujmović M, Lovasić I

Abstract – The study comprises 1358 patients who have undergone total vagotomy (TV) selective vagotomy (SV) with sec. Finney or sec. Heineke-Mikulicz.
Our descriptions of gastric morphology following TV and SV deviate from those reported in literature. Hypertonic wedgelike or horn – like forms dominate in a definite postoperative picture of the stomach. Otherwise, this shape is typical for SSV.
The appearance of pylorobulbar area corresponds to the one reported in literature with remark that pseudodiverticular protrusions of contours were represented to a much lesser ectent.
Hypotonia or spasm is found in the changed from of duodenal curve in 50% of the patients.

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Key words: vagotomy; pylorus-surgery, duodenum-radiography

Orig sci paper

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Introduction – Vagus resection and its influence on secretion and motility of the stomach have been known long ago. The surgical method in duodenal ulcer disease treatment by vagotomy combined with pyloroplasty as a drainage method is based on this cognition.

During radiological stomach and duodenum examination following vagotomy and pyloroplasty, the changed anatomical appearance can be the cause of difficulties in interpretion of the occurred morphological changes. It represents a great diagnostic problem not only for the less experienced radiologist, but even for the one with long roentgenologic experience if he is not familiar with the changes of anatomical relationships entailed by this drainage method. At present, we can look back at the analysis of definite X-ray changes of the stomach and duodenum from a longer time period.

Material and methods – During a 20-year period from 1965 to the end of 1984, 1358 patients with ulcer disease underwent vagotomy using one of drainage methods at the Surgical Clinic, Clinical Hospital Centre Rijeka.

Selective anterior and complete posterior vagotomies, combined with Finney's pyloroplasty, were carried out most frequently. This combination was applied in 974 examined patients (72%). Total anterior and posterior vagotomy with Finney's drainage method was performed 249 times and the Heineke-Mikulicz pyloroplasty 105 times. Other combinations were carried out in a lesser number of cases.

Radiological-anatomical appearance of the stomach has been conditioned by complex of symptoms as a whole, occurring in various combinations. The following was estimated: gastric shape and size, appearance of fundal gas bubble, secretion on an empty stomach, gastric emptying, tonus and gastric wall peristalsis.

The first (early) postoperative examination was performed in all the patients as a rule between the eighth and the tenth day following after surgery, after the nasogastric probe had been removed. Gastric and duodenal examination was managed in standing position of the patient. Examination of the complete gastric emptying was carried out between the fifth and the sixth hour after a contrast intake.

Not all the operated patients underwent the second (late) routine postoperative examination, but only those who appeared for a check up for some disturbances and those randomly called

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because of verification of the appearance and function following gastric vagotomy and pylorobulbar area. It was done within a long-time interval rangins from two months up to ten and more years.

Results – The dominance of symptoms on the first (early) control examination was as follows: a reduced tonus of the gastric wall, a stomach enlarging and on increased secretion on the empty stomach. Taking into consideration the expressive stage of the aforementioned symptoms all the examined patients were divided into two groups (Table 1).

The first group comprised the patients with less expressed symptoms. No retention of gastric contrast medium was observed during the second phase of the examination (60% of the operated examined cases).

Table 1 – Gastric form at the first (early) postoperative examination.

Group	Type	OPERATED PATIENTS No.	%	% forms within the first group
1	ty1	363	59,2	45,1
	ty2	260		32,3
	ty3	153		19,7
	ty4	23		2,9
		808		
2		554	40,8	
		1358		

The patients with strong retention and few cases of gastroplegia were included in the second group with markedly expressed symptom triad described. A high secretion column was above the contrast medium (40% of the operated examined patients (Fig. 2).

According to our experience four gastric types are distinguished in the first group.

Type 1 – characterized by a lesser curvature broken at a right angle in the angulus area. Vertical segment is usually narrower related to the wider horizontal one. No peristaltic waves are discerned along the lesser curvature. Fundal gas bubble is slightly enlarged (Fig. 1a).

Type 2 – a hook-like shape with clearly expressed longer and wider descending part and shorter and narrower ascending part. Small peristaltic waves of a dissimilar amplitude are better observed along the greater than the lesser curvature. Enlarged gastric fundal gas bubble is limited at the lower part by an ample level of liquid content being of greater horizontal than vertical diameter, just the same as in the remaining three gastric forms (Fig. 1b).

Type 3 – a horn-like shape with strong wall tonus, small fundal gas bubble, and the lower-

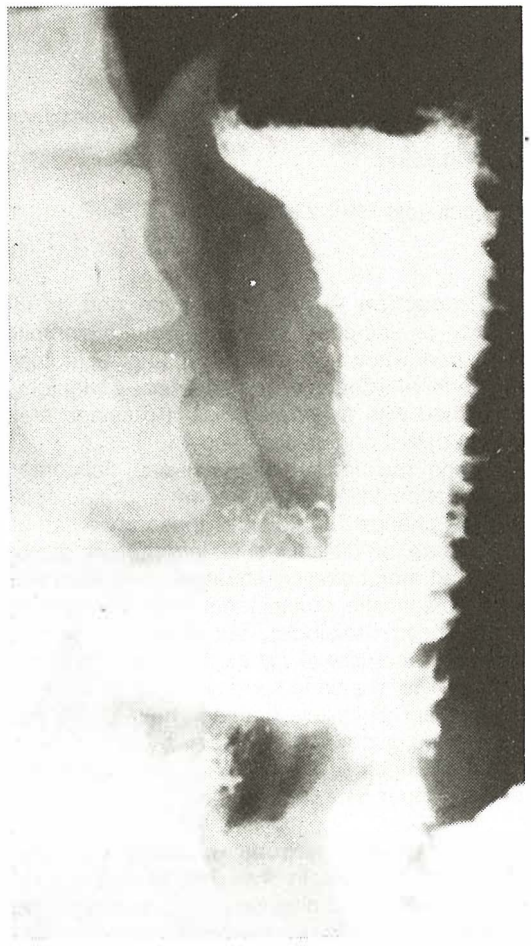

Fig. 1a – The stomach with broken lesser curvature at a right angle

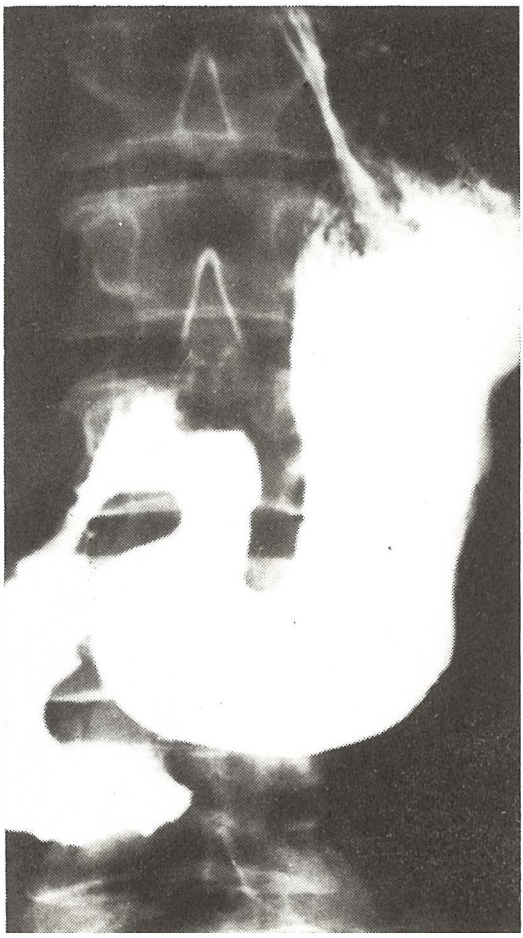

Fig. 1b – A hook-like stomach

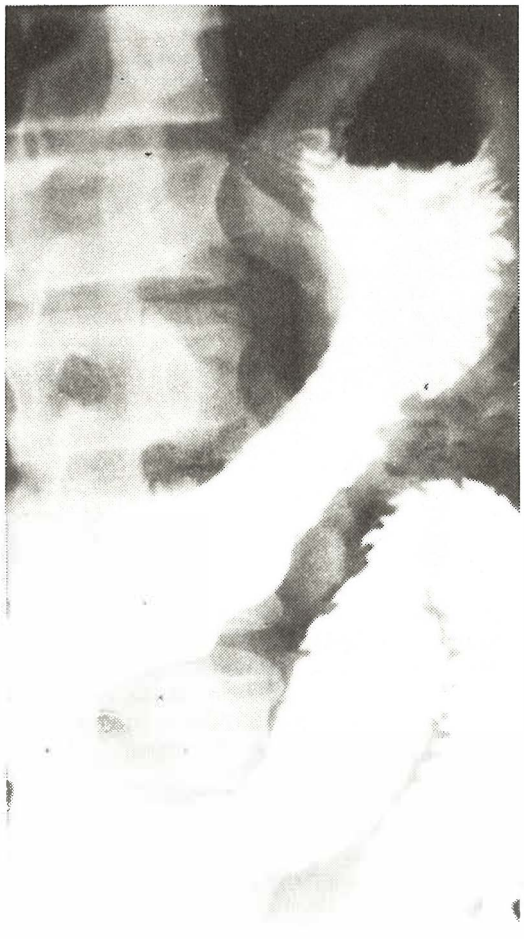

Fig. 1c – A horn-like stomach

most placed pylorobulbar part. This form was found less frequently and the contrast medium evacuation was accelerated (Fig. 1c).

Type 4 – a wedge-like shape with formed cascade in the area of relatively larger fundal gas bubble (Fig. 1d).

Estimation of secretion is possible on basis of secretion height column measuring and the level extension. Stimating the stage of secretion for the whole first group we are satisfied with conclusion it varies from completely empty stomach to hypersecretion of a medium degree. We didn't get involved in more accurate estimations for the quantity of secretion often increased in front of us during diascopy. A great amount of secretion was evident in the second group on an empty stomach, being often increased in the course of examination. Taken barium suspension decreased in the secretion like a »snow drop«, and the secretion was often mixed with food residues (alimentary retention).

The second (late) postoperative examination is characterized by regression of all radiological simptoms established during the first control examination. Hypersecretion and hypotonia gradually disappear to the end of the third and the fourth week after operation. Peristalsis becomes normal in this period. Those few cases of hypersecretion and hypotonia after this period completely vanish, according to our experience, to the end of the eighth week. Namely, radiological picture stabilizes, being definite from the sixth month onwards.

A turnabout of radiological picture, concerning the tonus, secretion and peristalsis is evident (Table 2). In all the examined cases wall tonus

Table 2 – Definite gastric form following vagotomy and pyloroplasty expressed on the sample of 120 examined patients. Comparison with control group of 120 inoperated examined patients without ulcus.

Group	Type	OPERATED PATIENTS		CONTROL GROUP	
		No.	%	No.	%
1.		22	18,2	17	14,0
		22	18,2	85	71,0
		23	23,2	17	14,0
		47	39,6	1	1,0
2.		1	0,8	0	0

was re-established and the increased secretion disappeared. Dividion into the first and the second group, as it happened during the first control examination, became unnecessary. Here all the examined operated patients who underwent follow-up were ranged into the first group.

There is also a complete turnabout of radiological gastric feature within the first group. All the examined patients display normal or increased wall tonus, regular rhythmical and symmetrical peristalsis, there is no secretion on the empty stomach at all, and the size of stomach is normal. Four gastric types described earlier in the first group are now represented in quite inverted numerical relationship. A wedge-shaped stomach with formed cascade or without it is most frequently found (39.6%), (Fig. 1d). Otherwise, this form is characteristic for the suprase-lective vagotomy (SSV). A horn-like stomach is in the second place (23.2%), (Fig. 1c). Both shapes are characterized by the lowermost placed part corresponding to plastic area. The lumen is gradually spread from this place to the fundus where the stomach is mostly extended, and the fundal gas bubble is more or less enlarged. This gas bubble is larger in the wedge-like stomach. A hook-like shape (Fig. 1b) and the from of a lesser curvature broken to a right angle (Fig. 1a) are equally represented (18.2%), but to a lesser extent, compared to the first two forms. The sinus is their lower-most part of the stomach. The stomach is empty before taking food in all the forms and the peristalsis is regular and

Fig. 1d – A wedge-like stomach

symmetrical. Peristalsis is absent or it is discernibly smaller only in a stomach with lesser curvature broken at a right angle. Therefore, such a form of gastric lesser curvature and the form of the stomach as a whole are thought to be caused because of the tonus difference alongside its one and other side as a consequence of the surgical treatment.

We had a good display of pylorobulbar area during the first control examination in approximately 60% of the examined patients. Some features, becoming typical during the second examination and later controls, appeared only individually. It was not possible to distinguish one type of the drainage operation from the other.

We always had good display of the whole duodenal curve including pylorobulbar area at the second control examination.

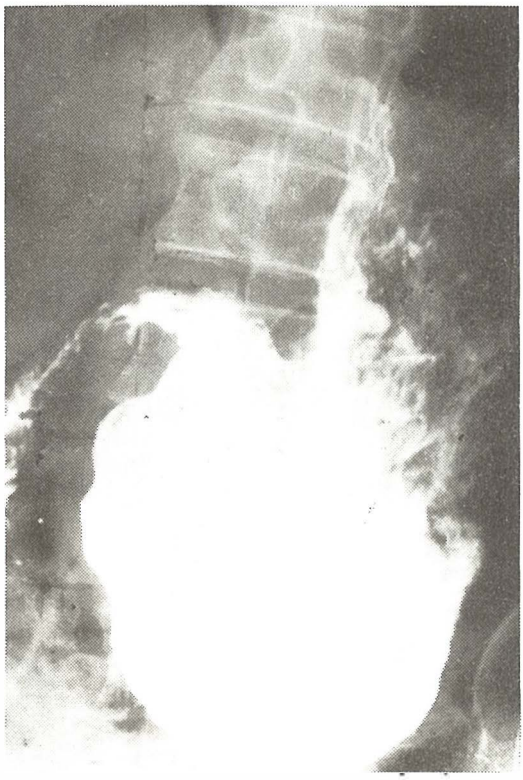

Fig. 2 – Ectatic, atonic ventriculus full of secretion on an empty stomach. A weak display of pylorobulbar area

At the Finney's drainage operation pylorobulbar area is characterized by a wide canal the gastric contrast medium is continuously moving through (Fig. 1b, 1d). Occasionally, there was an impression of passage discontinuity due to a gastric wall peristalsis and the position of the patient. Bulges of irregular and unusual shape can be observed on contours of both sides (Fig. 3a), and pseudodiverticulous formations are rarely found (Fig. 3b). Characteristic sign is more or less caused by the expressed ridge at the site of plastic, being visible as an impression of sharply bordered contour (Fig. 3c) and as a linear illuminated contrast shadow thrusting into the lumen from the side of greater curvature at the site of plastic. These both signs should be typical for the Finney's operation. Using a double-contrast technique the border of gastric and duodenal mucoust membrane can be often well observed. Spherical appearance of the outer contour of the upper and the descending duodenal part represents the third typical sign of this operation. Decrement of the duodenal curve

Fig. 3a,b,c,d – Typical changes of the form of pylorobulbar area and duodenal curve

appears as a result of wide junction between the stomach and duodenum (Fig. 1,2,3,4).

Wide junction between the stomach and duodenum with continuous passage of contrast medium have also been found at Heineke-Mikulicz operation. Contour at the site of plastic is usually protruded (Fig. 3d), while so many times mentioned and described pseudodiverticula (»Heineke-Mikulicz« diverticula or »dachshund ears«) (1,2,3,4,5,6) are not so much represented in our report (Fig. 4). Spherical outer contours of duodenal curve are expressed to a much lesser extent than at Finney's operation (Fig. 4).

The remaining part of duodenal curve is of equal appearance regardless whether it is a question of one or another type of pyloroplasty. Continuous filling of the whole duodenal curve is

Fig. 3b

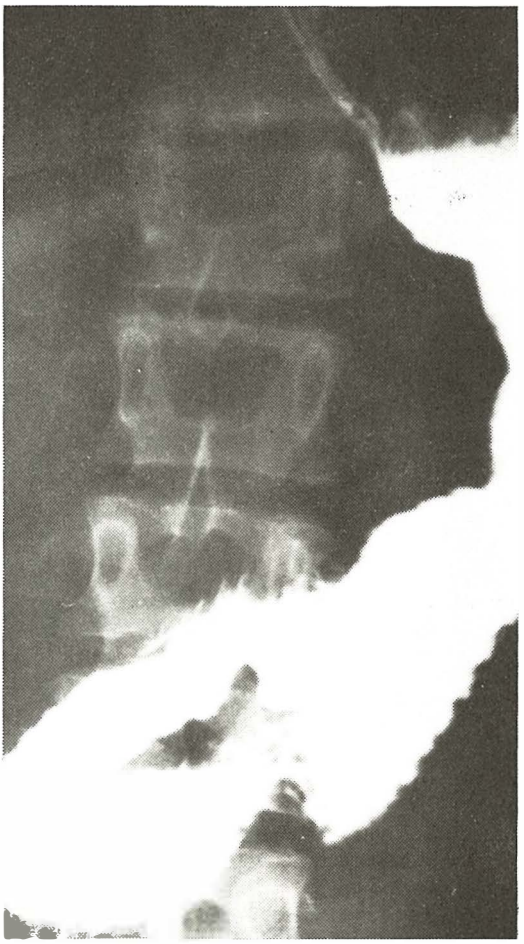

Fig. 3c

found in approximately 50% of the patients by demonstration of mucosal configuration (the picture of »watering-can«) (Fig. 1b). Narrower lumen accompanied with lesser or stronger expressed spasm is present in 25% of the patients. Often findings are edematous, inflammatory changed mucosal folds (Fig. 5a). Pronounced hypotonia with occasionally visible antiperistaltic waves is present in the remaining one fourth (Fig. 5b).

Discussion – Without getting into details, Beeger and Vogel (1) report stomach enlarging, reduced peristalsis with uncoordinated contractions and slow evacuation in the truncal vagotomy (TV). Changes in the selective vagotomy (SV) are identical to those in TV, but with earlier regression. It primarily aplies to re-establishment of tonus, following in the third or the fourth week, but not later than the third month.

Sapounov (3) reports in detail the gastric picture following vagotomy (SV) based on 400 operated and examined patients. He describes normal appearance of the stomach and neat emptying in 56% of patients. A wedge-like form of corpus and fornix, typical for SSV, with neat emptying is found in 25% of patients. 18% of patients developed ectasy with slow evacuation. Gastroplegia is observed in 2.5% of patients.

Comparison of the forms found, and general appearance of the stomach is neither possible nor authoritative at the first examination because of various types of vagotomy and pyloroplasty and their mutual combinations (1,2,4,5,6,7,8). According to the description of the stomach appearance our finding are more similar to those

Fig. 3d

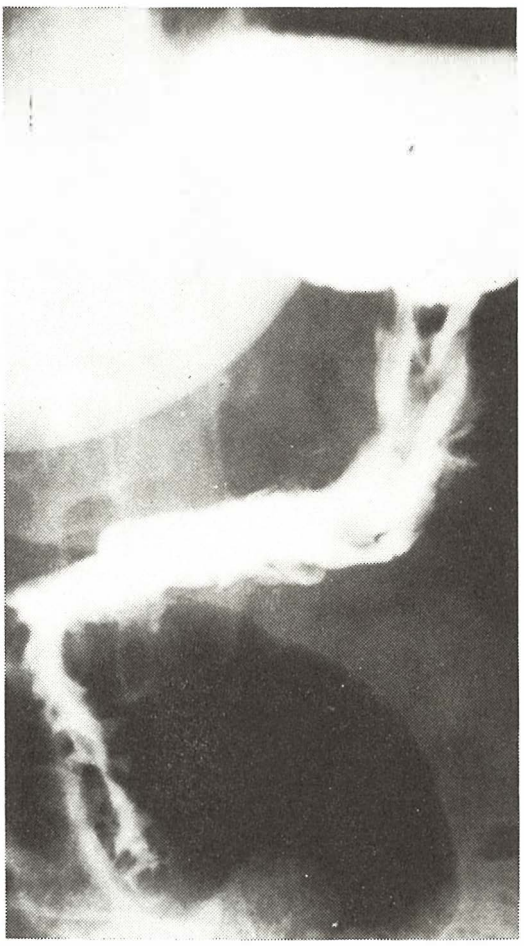

Fig. 4a – Spastic form of the duodenal curve

described by Sapounov (3), being essentially dissimilar in the number of particular findings. »Normal finding« and marked ectasies and hypersecretions with normal evacuation are much more represented in his findings (80%). The difference in the appearance of the antral part of the stomach is even greater. Relatively narrow antrum has been found by Sapounov in the equal percentage (80%). Namely, he considers the patient with ulcus to have dysfunction of antral wall and the pyloric canal caused by fibromuscular hypertrophy, inflammatory infiltration and degenrative nervous changes. Vagotomy is followed by more or less expressed muscular decompensation of other parts of the gastric wall. We should also favour this explanation since we found such findings in those patients who had undergone bilateral TV. In addition, such appearance of the stomach in patients who underwent SV could be caused by a higher rate of innervation coming sometimes from gastric collaterals of the hepatic vagal branch.

Some authors try to judge the achieved success in vagotomy even in the early phase of examination based on the assessment of picture elements and gastric function (1,4). We do not agree with it because we noticed many turnabouts concerning the form and function, especially in the control abdominal picture six hours later.

Those, being engaged in these problems (1,2,3,4) usually speak about the postoperative normalization from one to two months without getting into a more detailed description of mor-

Fig. 4b – Hypotonic form of the duodenal curve

Fig. 5a – Markedly expressed postbulbar stenosis

phological changes. We should not agree with general statement that the stomach assumes its typical preoperative shape. Table 2 lists numerical relationships among gastric types in inoperated persons. Percentage differences in representation of particular types of the stomach in comparison to their representation following vagotomy and pyloroplasty are obvious.

Greater representation of hypotomic gastric shape (type 3 and type 4) certainly results from changed innervation. Residual vagal branches after incomplete vagotomy can explain hypertonia in the early postoperative phase. Later, a certain role is likely to play in it by intramural nerve plexuses.

From our experience, no definite assessment about efficiency of a drainage operation can be made in either type of pyloroplasty according to the appearance of pylorobulbar area during the first follow-up examination, because of accompanying symptoms conditioned by oedema, spasm, hypotonia and secretion.

All the morphological and functional changes in the whole duodenal area are of temporary character, being essentially changes as the time passes on after the operation. These changes result from the wall consolidation at the site of sutures, oedema disappearance and cicatrical changes during tonus re-establishment in the wall.

Šepić (9) and Zaninović (10) report sec. Finney to give better technical possibilities for lumen distension (Fig. 5a, 5b), especially in the case of very strait lumen owing to cicatrical changes. Sapounov (3) quotes that finding of normal or slightly ectatic pylorus with normal bulbar basis means unsuccessful pyloroplasty. We had several finding of a kind and decided to support the statement reported (Fig. 6).

Fig. 5b – The same patient following Finney's pyloroplasty. Wide gastroduodenal canal at the site of stenosis.

Fig. 6 – Preserved form of the bulbus and pylorus as a sign of inadequate pyloroplasty. The sign of ridge is placed aborally to the bulbus.

All the gastric and duodenal examinations after vagotomy and pyloroplasty are easy to carry out, and do not require special technical conditions. Making comparisons of the reports by various authors is very difficult or not practical at all. The reason for this is diversity of methods of vagotomy and pyloroplasty and their all possible mutual combinations.

Investigation of radiological anatomy of the stomach and duodenum after truncal and selective vagotomy with pyloroplasty, regardless the recently more and more applied proximal selective vagotomy, is of great importance. It is a fact that the operated in such a way are among our patients, and there is always a risk for a radiologist, who is not experienced enough, to interprete radiological-anatomical picture in a wrong way.

Sažetak

RADIOLOŠKA ANATOMIJA ŽELUCA I DVANAESNIKA POSLIJE VAGOTOMIJE I PILOROPLASTIKE

U studiji je uključeno 1358 pacijenata u kojih je učinjena TV il SV uz sec. Finney ili sec. Heineke-Mikulicz.

Naši opisi morfologije želuca nakon trunkalne ili selektivne vagotomije odstupaju od opisa u literaturi. U definitivnoj slici želuca poslije operacije dominira hipertonična forma u obliku klina ili roga. Ovaj oblik je inače tipičan za SSV.

Izgled pilorobulbarnog područja odgovara opisima u literaturi uz napomenu da su mnogo manje zastupljena pseudodivertikulozna izbočenja kontura.

U promijenjenoj formi duodenalnog zavoja kod polovice slučajeva nalazimo hipotoniju ili spazam.

Uočene su razlike forme kod istih drenažnih metoda a različitih timova operatera.

References

1. Beeger F, Vogel H. Röntgenmorphologie nach Vagotomie, Röntgen Bl 1983; 36:403-6.

2. Maas R, Vogel H. Die Röntgenmorphologie des Magenausgangs nach Pyloroplastikoperationen. Fortschr Röntgenstr 1982; 137(4):428-33.

3. Sapounov S. Das Röntgenbild von Speiserohre, Magen und Zwölffingerdarm nach selektiver gastraler Vagotomie und Pyloromyoplastik. Fortschr Röntgenstr 1971; 115:423-32.

4. Stauch G, Lohr E, Boettcher I, Beersiek F, Eigler FW, Das Röntgenbild des Magens und Zwölffingerdarmes nach organschonender Operationen beim Gastroduodenalulkus. Fortschr Röntgenstr 1974; 120:31-41.

5. Dihlmann W, Cen M. Zur Kennthis und röntgenolgischen Beurteilung der Drainageoperationen am Magen. Der Radiologe 1969; 6:196-200.

6. Jamakoski B, Novak J, Peev A, Serafimov K, Ivanov A. Rentgenološki, morfološki i funkcionalni karakteristiki na gastroduodenumot posle proksimalna gastrična vagotomija. In: Zbornik radova I. naučnog sastanka, Vagotomija u liječenju gastroduodenalnog ulkusa, Opatija 1978; 297-305.

7. Eideshem D, Otteni F, Hollender LF, Bloch P. Etude des aspects radiologiques de l'estomac dans le decours immediat d'une vagotomie supra-selective. J Radiol Electrol 1975; 56(12):841-6.

8. Zeitler R. Röntgendiagnostik des operierten Magens. Der Radiologe 1969; 173-86.

9. Šepić A. Vrijednost vagotomije i piloroplastike u liječenju perforiranog duodenalnog ulkusa. Disertacija. Rijeka 1974.

10. Zaninović N, Švalba N, Komljenović B, Gudović A, Zelić A, Frančišković V. Analiza i rezultati vagotomije i piloroplastike u liječenju ulkusne bolesti. In: Zbornik radova I naučnog sastanka Vagotomija u liječenju gastroduodenalnog ulkusa Opatija 1978;31-9.

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SUPERIOR MESENTERIC ARTERY (SMA) ANEURYSM WITH A MARFAN SYNDROME – CASE REPORT

Radanović B.[1], Šimunić S.[1], Borčić V.[2], Oberman B.[1], Strozzi M.[3], Škegro M.[2]

Abstract – A case of an aneurysm of the superior mesenteric artery trunk with a Marfan syndrome suggested by real-time ultrasound and CT confirmed by angiography is presented.
Surgical resection of the aneurysm was successfully performed.

UDC: 616.136.44-007.64:616.71-007.152

Key words: mesenteric arteries; aneurysm; Marfan syndrome

Case report

Radiol Iugosl 1991; 25:297-9.

Introduction – Aneurysms of superior mesenteric artery (SMA) trunk and its branches are very rare. In surgical and radiological literature they are described as sporadic cases or only in smaller series (1,2,3,4).

Etiological factors causing the SMA aneurysms are arteriosclerosis, trauma, inflammation, medial cystic necrosis, collagen vascular diseases, arteritis, hepatic, lesions and congenital anomalies (3,4,5). Their frequencies are best illustrated by works of Lucke & Rea and McNamara (1,4).

Most often asymptomatic, in case of rupture, they are followed by bleeding into the gastrointestinal or peritoneal tracts. Non-invasive radiological diagnostic methods (US, CT, MRI) reveal the SMA aneurysms most often as an expansive process in the irrigational part of SMA, with stronger or slighter suspicion for aneurysm. Only the angiographic examination – conventional or digital subtraction angiography (DSA) – provides a complete morphological and hemodynamic display of aneurysm. Angiographic finding of aneurysm with its relation to the trunk, a display of peripheral ramification and possible collateral are the basic conditions for a successful surgical intervention (4,5,6,7).

Case report – A 22-year old woman was treated from her earliest childhood for a mitral orifice insufficiency caused by a prolapse of mitral valve. The patient was extremely high (194 cm), a Marfan constitution with dolichostenomelia and arachnodactilia and with a high gothic palate. Ophthalmologic report was in order. Six months earlier she was treated for endocarditis with bacterial vegetations on both mitral cusps and positive hemocultures (alpha-hemolytic streptococcus). A month later, she developed waist epigastric pains with no nausea or vomiting. Pain decreased in a bent sitting position.

Laboratory findings were within normal range. Arterial blood pressure was normal. Palpation of the umbilical region discovered a well formed, smooth round pulsatory formation 7-8 cm of size.

Ultrasound examination revealed a cystic mass of 5.0 x 7.0 cm in para-aortal abdomen. Systolic flow from the aorta was evident by Doppler method. CT examination showed a massive round expansive formation fo fresh blood absorption values.

The abdominal aortography established a good state of celiac, renal and inferior mesenteric arteries. However, a clear survey of SMA and its

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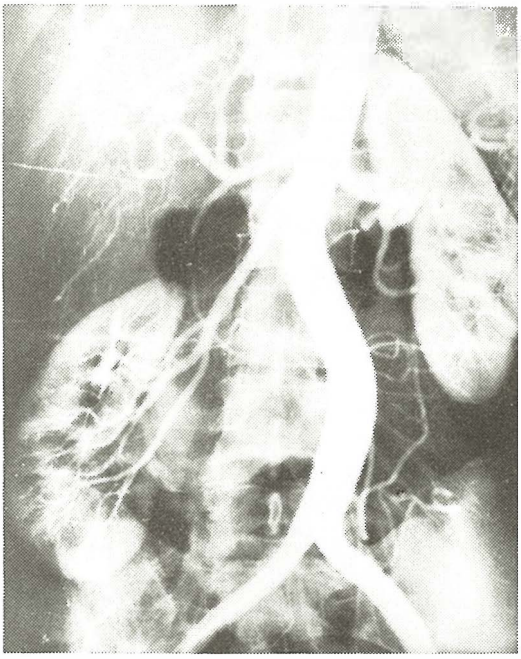

Fig. 1 – Abdominal aortography: the absence of SMA picture, pale contrast opacity right para-aortal

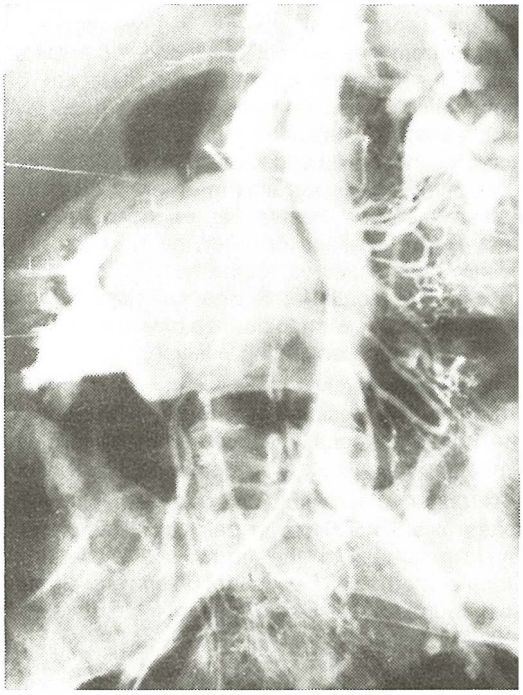

Fig. 2 – SMA selective angiography: a huge aneurysm

branches was missing. In later stage, a pale contrast opacity about 7-8 cm on the right side was observed causing the impression of subrenal part of the abdominal aorta. Only the selective angiogram of SMA offered a clear picture of SMA trunk with its branches and a huge aneurysm of about 8.0 cm in approximately 10.0 cm of SMA from the aorta. Jejunal branches appeared to be normal. Collaterals from jejunal branches and mesenteric arcades also showed a post-aneurysmal part of SMA and its branches. In later stage, the mesenteric-portal vein system was neatly presented (Figs. 1 and 2).

Immediately after the angiographical diagnostic examination, a surgery followed with extirpation of the aneurysm (Fig. 3).

Initial and subsequent post-operative recovery was normal. Histological finding revealed a granulated tissue and smaller formations of lymphocytes and macrophages in arterial and aneurysmal walls.

Three months later, control DSA was performed. The abdominal aortography did not show the SMA trunk, and left colic artery and inferior mesenteric artery (IMA) formed a hypertrophic Riolan arch. On selective celiac trunk angiogram a hypertrophic gastroduodenal artery and broad pancreatic duodenal arcades were found, over which the postocclusal SMA segment was vascularized (Figs. 4 and 5).

The patient has been, without subjective or objective difficulties.

Discussion – First successful resection of SMA aneurysm was performed by DeBakey and Cooley (1949) and marked the turn in surgical treatment of this disease (3).

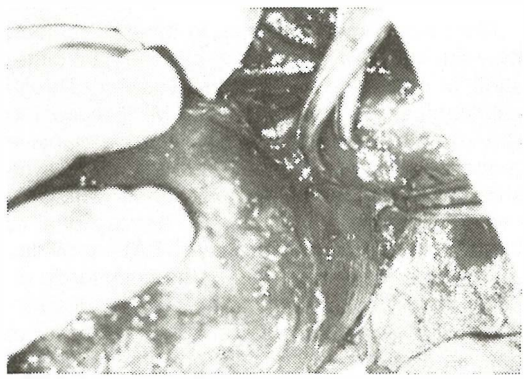

Fig. 3 – Intraoperative display of SMA aneurysm

Fig. 4 – Post-operative DSA of the abdominal aorta: SMA trunk display missing, hypertrophic gastroduodenal arcades, Riolan arch.

Fig. 5 – Post-operative selective DSA of the common hepatic artery: hypertrophic gastroduodenal artery and pancreatic duodenal arcades: revascularization of a postocclusive SMA segment.

Precise pre-operative diagnostic examination stands as a basic condition of a well planned and performed surgical treatment. The most important part in a diagnostic algorithm of this disease is attributed to the angiographic examination (3, 4, 5).

Arteriosclerosis participates as the most frequent factor in the etiopathogenesis of SMA aneurysms. Other factors are rare (3, 4, 5).

In our case, we had a young patient with a Marfan syndrome and a predominant cause of huge aneurysm was most probably due to a congenital disorder of connective tissue, yet subacute bacterial endocarditis the patient underwent could not be disregarded.

Surgical resection of the aneurysm was successfully performed. Post-operative DSA showed significantly changed hemodynamic situation in the irrigating part of SMA (the occlusion of the starting segment with hypertrophic pancreatic duodenal arcades and Riolan arch), but without clinical signs of mesenteric ischemia.

Sažetak

ANEURIZMA GORNJE MEZENTERIČNE ARTERIJE SA MARFANOVIM SINDROMOM – PRIKAZ SLUČAJA

Prikazan je slučaj bolesnice s Marfanovim sindromom i aneurizmom gornje mezenterične arterije, koja je dijagnosticirana ultrazvukom, kompjutoriziranom tomografijom i angiografijom. Kod bolesnice je uspješno izvedena kirurška resekcija aneurizme.

References

1. Lucke B and Rea MH. Studies on aneurysm: general statistical data on aneurysm. JAMA 1921; 77:935-40.
2. Graham JM, McCollum CH, DeBakey ME. Aneurysms of the splanhnic arteries. Am J Surg 1980; 140:797-801.
3. DeBakey ME, Cooley DA. Successful resection of mycotic aneurysm of superior mesenteric artery: case report and review of literature. Am Surg 1953; 19:202-12.
4. McNamara MF, Bakshi KR. Mesenteric aneurysms. In: Bergan JJ, Yao JST, eds. Aneurysms: diagnosis and treatment. New York: Grune & Stratton, 1982:385-403.
5. Knox M, Chuang VP, Stewart MT. Superior mesenteric aneurysm and arteriovenous fistula: angiographic and CT features. AJR 1985; 145:383-4.
6. Baker KS, Tisnado J, Cho SR, Beachley. Splanhnic artery aneurysms and pseudoaneurysms: transcatheter embolization. Radiology 1987; 163:135-9.
7. Mourad K, Guggiana P, Minasian H. Superior mesenteric artery aneurysm diagnosed by ultrasound. Br J Radiol 1987; 60:287-8.

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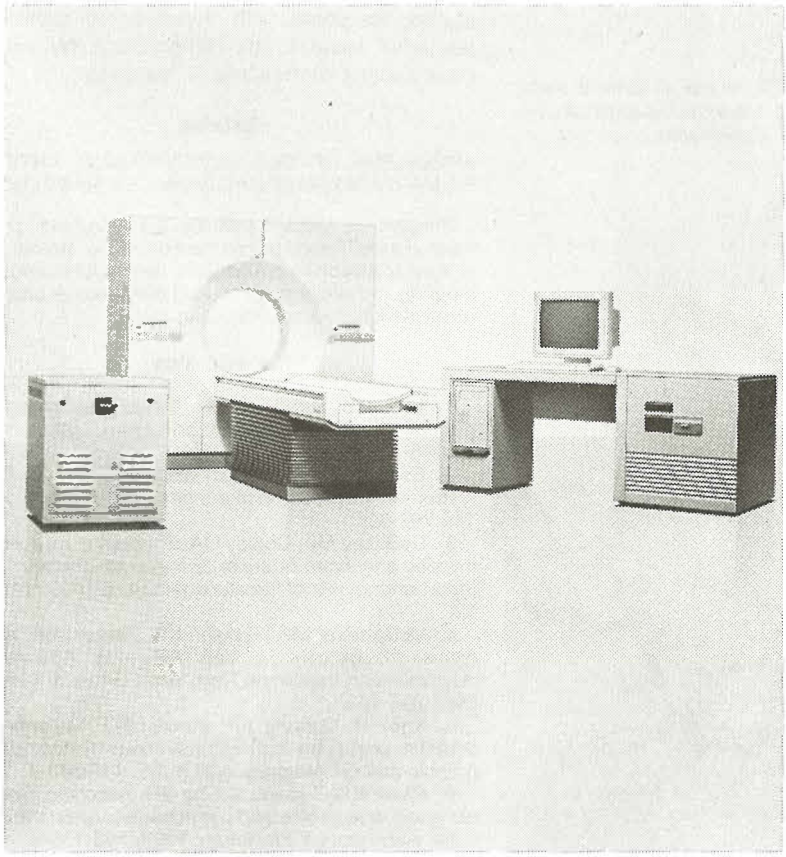
SIEMENS

SOMATOM AR.T

Ganzkörper-Computertomograph

SIC 212

CT



INSTITUTE OF RADIOLOGY UMC NIŠ

INTRAARTERIAL DIGITAL SUBTRACTION ANGIOGRAPHY OF THE INTRACRANIAL BLOOD VESSELS – IMAGING COSTS ANALYSIS

Bošnjaković P, Ivković T, Ilić M, Milatović S, Ivković A

Abstract – We compared the costs of standard neuroangiographic procedures with the costs entailed by digital arteriographic imaging. A prospective study was performed in 1989, including 50 patients with subarachnoidal hemorrhage in each group. The study resulted in 29.8% cost reduction in catheterization and filming material in favour of digital subtraction angiography (DSA). The procedure with DSA lasted significantly shorter. More projections were required with DSA because of flexibility and simplicity of the method. If connected with two angiographic machines, DSA would be completely payed back in 1 year.

UDC: 616.831.94-002.252:616.133.33-073.75

Key words: subarachnoid hemorrhage; angiography, digital subtraction

Orig sci paper

Radiol Iugosl 1991; 25:301-3.

Introduction – The method of Digital Subtraction Angiography (DSA) has been developed for visualization of the arterial side of circulation after intravenous injection of contrast medium in bolus, but the full application in neuroradiology was achieved with intraarterial injections after selective catheterization (1, 2, 3, 4). Beside the parameters related to the quality of the picture and diagnostic value of the study, those that show the costs of application method, compared with the costs of standard angiographic technique, are of importance (9, 7). In order to determine these factors we performed a prospective study comparing the imaging costs in groups of patients examined with DSA and conventional angiography. Based on the results of the study, we estimated the time necessary for the DSA unit to pay back.

Material and methods – The study was performed in the Institute of radiology UMC Niš, Yugoslavia between January and December 1989.

Fifty patients with clinical and computer tomographic signs of subarachnoidal hemorrhage were examined by means of DSA whereas 50 others with the same symptoms were examined by automatic puck film changer. In both groups, we were measuring duration of the intervention, number of projections obtained, necessary material for catheterization and filming. Afterwards we compared the values.

All the examinations were performed on an Angioscop C X-ray unit (Siemens) with Coordinat IIID table, puck film changer which accepted the 24 x 30 size of films. The DSA group was examined using the Angiotron CMP (Siemens) which started to function in our institution in June, 15th, 1985. The matrix size was 512 x 512 and image intensifier diameter 33 cm. The documentation of the angiographic findings was achieved on single-emulsion films using multiformat camera. Interventional procedures were not analyzed.

The costs were calculated considering the number of films used per patient, the amount and concentration of contrast medium and necessary catheterization material.

On the basis of the number of examined patients during 12 months and knowing price of a DSA unit, the time necessary for the machine to pay back was calculated.

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Results – Examination time necessary for the visualization of both carotid and vertebrobasilar artery arborization, measured from the puncture of the femoral artery to catheter evacuation, was significantly shorter with DSA (50,14 minutes) compared with conventional angiography (89,56 minutes) owing to the elimination of the time necessary for the photographic film processing. This fact opens the possibility of examining more patients during the daily work.

The number of obtained projections was higher in the group of patients examined with DSA (7,80 : 7,12). The reason is flexibility and rapidness of aquiring the additional projections with DSA.

The structure of catheterization material and contrast media is shown on table 1 (prices in DEM).

Table 1 – Costs of the examination per patient (DEM)

Material	DSA	PUCK
catheter	42	42
quide wire	29	29
film	51,6	75
contrast medium	79,4	141,7
Total	202	287,7

The costs for guide wires and catheters in both groups were the same. The film costs in DSA group comprised 12 single-emulsion films (24 x 30). This number of films was used with only one DSA picture per film which was best accepted by neurosurgeons. For contrast medium cost analysis, the mean price of 50 ml of nonionic contrast medium, at a concentration of 300 mg/ml was calculated.

In the group of patients examined with standard angiographic technique, beside guide wire and catheter, we calculated the costs of 30 films (24 x 30) and 80 ml of nonionic contrast medium at a concentration of 30 mg/ml or higher.

The application of DSA resulted in 29.80% cost reduction per patient.

Taking in account the price of the unit of 250 000 DEM and the price of automatic puck film changer, with supposed frequency of 1000 patients per year, the unit would pay back in less than two years. The units of latest generations are more expensive so, with the price of 750 000 DEM per unit, pay back time would be 7,5 years, amortization and interests not included.

The pay-back time could be reduced to half the time if the unit is connected with two angiographic machines.

It should be pointed out that the greatest cost reduction could be achieved in interventional procedures which are not included in this study.

Discussion – By means of DSA the intracranial vasculature might be visualized in three ways: after intravenous injection of contrast medium in bolus (with central or peripheral injection), after semiselective injection in the aortic arch and after selective catheterization of the vessel (5). Each of the methods mentioned above has advantages and disadvantages, but intraarterial injection after the selective catheterization is widely accepted because of image quality, absence of artefacts, and superposition and dependance on the cardiac function (6).

The main drawback of the DSA image achieved with intraarterial injection is less spatial resolution if compared with conventional angiographic films. This is more obvious in visualization of the small vessels (smaller than 0.5 mm in diameter). Using matrix size 1024 x 1024 and TV systems with 1000 lines on the monitors and cameras, the spatial resolution will be significantly improved and new fields for the application of DSA technique opened. The machines with such characteristics are more expensive compared to the machines of the first and the second generation (7).

Because of the differences in duration of the procedure, speed of image acquisition and used material, literature data show cost reduction in favor of DSA between 10 and 30 percent (7). Cost reduction is estimated to be 200 USD per patient by Brandt-Zawadzki et al. (8).

It should be emphasized that our study showed the expenses in a single X-ray tube unit. The biplane unit, in our oppinion, would not result in significant shortage of neuroangiographic procedure. The amount of contrast medium would be reduced, but in other parameters (including the unit price) there would not be any important difference.

Conclusion – Intraarterial DSA, after selective catheterization, is very important in neuroradiology and can almost completely (except neovasculature assesment) replace conventional angiography. Beside the advantages in manipulation with the unit and image quality, important factor is the cost reduction which is aproximately 30 percent in favor of DSA.

Sažetak

INTRAARTERIJSKA DIGITALNA SUPTRAKCIONA ANGIOGRAFIJA INTRAKRANIALNIH KRVNIH SUDOVA – ANALIZA TROŠKOVA PRIMENE METODE

Uporedili smo troškove primene standardnih neuroangiografskih procedeura sa troškovima pregleda uz primenu digitalne suptrakcione angiografije (DSA). Prospektivna studija izvedena je 1989, godine sa po 50 bolesnika sa znacima subarahnoidalne hemoragije u svakoj grupi. Rezultati su pokazali sniženje troškova kateterizacionog i filmskog materijala za 29.80% uz primenu DSA. Ušteda u vremenu uz DSA je značajna. Uz DSA bio je korišćen veći broj projekcija po bolesniku zbog fleksibilnosti i lakoće primene. Ukoliko je povezana sa dva angiografska aparata DSA će se kompletno isplatiti za godinu dana.

References

1. Robb GP and Steinberg I. Visualization of the chamber of the heart, the pulmonary circulation and great blood vessel in man. AJR 1939; 41:1.

2. Bannister RG, Leslise M. Venoangiography in the study of cerebrovascular diseases. Brain 1963; 86:161.

3. Kruger RA, Mistreta CA, Houk TL et al. Computerized fluoroscopy techniques for intravenous study of cardiac chamber dynamics. Invest Radiol 1979; 14:279.

4. Bošnjaković P. DSA in diagnosis of intracranial aneurysms and arteriovenous malformations (doctoral thesis). University in Niš 1990; 68-79.

5. Zimmerman RA, Grossman RI, Goldberg HI et al. Comparation of digital subtraction angiography with conventional film screen subtraction arteriography for neuroradiology. Neuroradiology 1984; 26:457-2.

6. Nakstad D, Bakke SJ, Kjartansson O. Intra-arterial digital subtraction angiography of carotid arteries. Special refference to contrast media. Neuroradiology 1986; 28:195-8.

7. Norman D, Ulloa N, Brandt-Zawadzki M. Intraarterial Digital Subtraction. Imaging costs consideration. Radiology 1985; 156:33-5.

8. Brandt-Zawadzki M, Gould R, Norman D. Digital subtraction Cerebral angiography by intraarterial injection: comparation with conventional angiography. AJNR 1983; 347-53.

9. Modic MT, Weinstein MA, Chilcote WA et al. Digital subtraction angiography of intracranial vascular system: comparative study in 55 patients. AJR 1982; 138:299-306.

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MILITARY HOSPITAL ZAGREB, DEPARTMENT OF RADIOLOGY
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DIGITAL SUBTRACTION SIALOGRAPHY

Borković Z, Katić B, Ožegović I

Abstract – The technique of sialography of the parotid gland by means of digital subtraction has been applied in 19 patients. We have done both sides in 2 patients, so the total number of investigations performed was 21. The diagnoses were confirmed by clinical, cytological aspiration biopsy or also by histological findings after surgery. Sialography by means of digital subtraction is a diagnostic improvement in comparison with classical sialography because of its higher resolution and the ability to show details. The subtraction of bone structures, as well as of air in the pharynx and sinuses, enables clearer imaging of the salivary gland duct and the gland itself. Using this method, a large number of recordings can be obtained, and the images improved by digital processing; it is most important, though, that the dose of radiation is significantly reduced.

UDC: 616.316.5-073.755

Key words: sialography-methods; parotid gland

Profess paper

Radiol Iugosl 1991; 25:305-7.

Introduction – The method of digital subtraction angiography is applied for review of nonvascular structures of the parotid gland.

This method for visualisation of the parotid gland, parotid duct, intraductal changes and a review of the salivary gland tissue by application of digital technique has been developed to make the diagnosis by means of digital subtraction sialography more simple and useful (1-4).

With the diagnostic methods of CT, CT–sialography, MR, US and digital subtraction sialography, the latter method opens new possibilities in the diagnosis of pathological changes in the imaged structures (4–9).

Because of the large number of recordings, arithmetical processing and the applied technique of subtraction reinforcement of signal, reduced time needed for examination and a reduced dose of radiation, this method has proved to be superior in comparison with classical film method (3).

Materials and methods – During our three year study of digital subrraction sialography, 19 patients were examined: one 47-year old woman and 18 men 19-62 years of age. The proportion of examined salivary glands on the left and on the right side was the same. Bilateral examination of the parotid glands was performed in 2 patients; there was a pause of one day between both examinations.

All the examinations were done by means of a Philips DVI–CV machine with application of an electronic amplifier 6 and 10 in. of size. Sideways recordings were taken in all patients. We performed 21 recordings for each patient with the application of contrast medium and the patient in lying position; the speed was 1.9 recordings per second. This examination requires a good cooperation of the patient as he has to stay calm for 15 seconds.

The contrast medium was applied manually, using a needle with rounded tip or a catheter SIA-30 (Angoimed). Non–ionic contrast medium Iohexol (Omnipaque 180-Nycomed) in a quantity of 2–6 ml was used. The application of contrast medium during the recording was followed on the monitor till the review of glandular phase.

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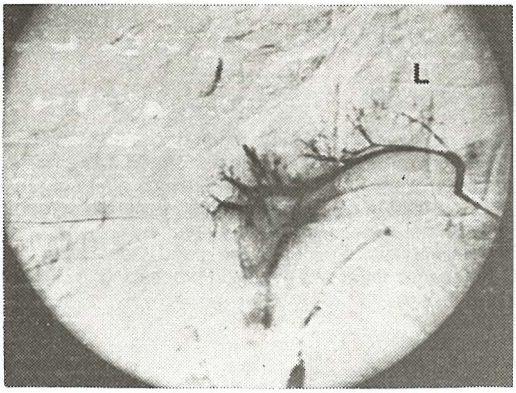

Fig. 1 – Chronical sialadenitis of the parotid gland

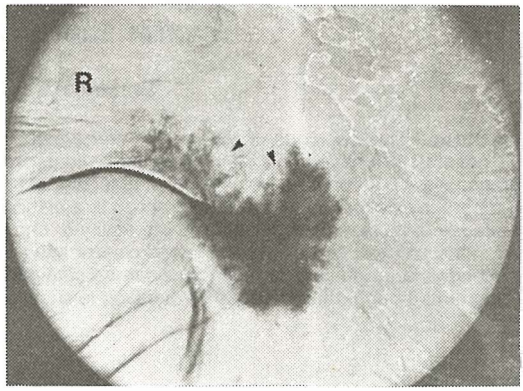

Fig. 2 – Infiltration of the proximal part of the parotid gland with a malignant tumor (arrow)

Results – The method of digital subtraction sialography was applied in 19 patients. Two od them had bilateral examination which gave a total of 21 digital subtraction sialographies.

The results are shown in Table 1. There were 7 patients whose findings were within the limits of normal values. In 5 patients chronic inflammatory changes were found which were expressed as obvious dilatation and rough contours of the parotid duct, but at its narrow elongated end it was tortuous, displaced or bowed (Fig. 1). Branches were considerably reduced and irregularly formed. Glandular phase showed a reduction of glandular tissue. Benign lipoma showed a sharply delineated defect in the glandular tissue.

We found a central or peripheral defect in the glandular tissue in malignant lymphoma and malignant epithelioma which had wavy polycyclic contours (Fig. 2). In all patients the diagnosis was established by cytological aspiration biopsy and pathohistological examination of surgical specimens (Table 1).

Table 1 – Digital sialography, clinical and pathologic diagnosis

Diagnosis	No. of patients
Normal glands	7
Chronic sialoadenitis	5
Abscess	2
Lipoma	1
Lymphoma	2
Epithelioma	2
Total	19

Discussion – The ditital subtraction sialography represents a new technique for extravascular review of the parotid duct and the parotid gland. The method can be regarded as a considerable improvement because of its ability to show even very small structures and intraductal changes better than the classical sialography. In the latter method, the intensity of bone shadows and air in the pharynx substantially interfere with correct interpretation of the findings.

By using the non–ionic contrast Iohexol (Omnipaque 180) in a small quantity and by following the contrast medium till the optimal review, we get a high quality image on the monitor and we also avoid striking sensations in the area of the facial nerve.

The method of digital subtraction sialography represents a considerable diagnostic improvement in comparison with the classical sialography.

The examination has several advantages: it does not require much time, the image obtained is better, a lesser quantity of contrast medium is needed, and, as the most important, the dose of radiation received by the patient during examination is reduced.

References

1. Dawson P. Digital Subtraction Angiogprahy–A Critical Analysis. Clinical Radiology 1988;39:474-7.
2. Lightfoote JB, Friedenberg RM, Smolin MF. Digital Subtraction Ductography. AJR 1985;144:635-8.
3. Gmelin E, Rinast E, Bastian GO, Hollands – Thorn B, Weiss HD. Dakryzystographie und Sialographie in digitaler Subtraction. Fortschr. Röntgenstr 1987;147:643-6.

4. Cizmeli E, Ilgit ET. The technique and advantages of digital subtraction sialography. European Congres of Radiology, Vienna 15-20 sept. 1991 p. 291.

5. Iko BO. Computed Tomography and Sialography of Chronic Pyogenic Parotitis. Br J Radiol 1984;57:1083-90.

6. Mc Gahan JP, Walter JP, Bernstein L. Evaluation of the Parotid Gland: Comparison of Sialography, Non-contrast Computed Tomography and CT sialography. Radiology 1984;152:453-8.

7. Eviolfsson O, Nordshust T, Dahl T. Sialography and CT Sialography in the Diagnosis of Parotid Masses. Acta Radiol (Diagn) 1984;25:361-4.

8. Gritzman N. Sonography of the Salivary Glands. AJR 1989;153:161-6.

9. Bohnodorf K, Lönnecken I, Zanella F, Lanfermann L. Der Wert von Sonographie und Sialographie in der Diagnostic von speicheldrüsenerkrankungen. Fortschr. Rötgenstr. 1987;147:288-93.

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Case 4

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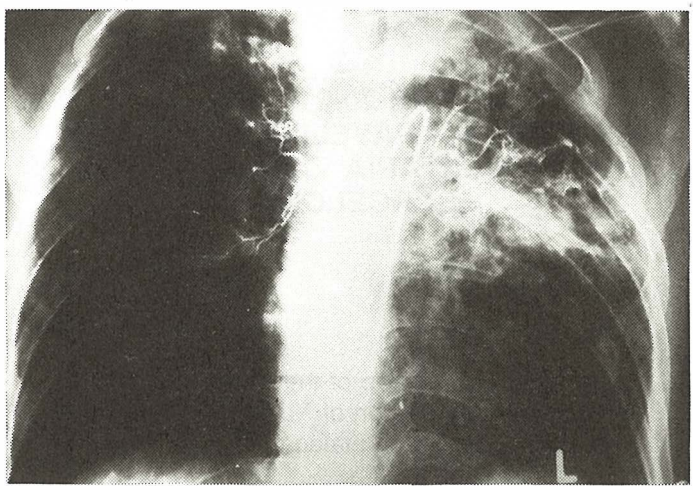

Figure 1a

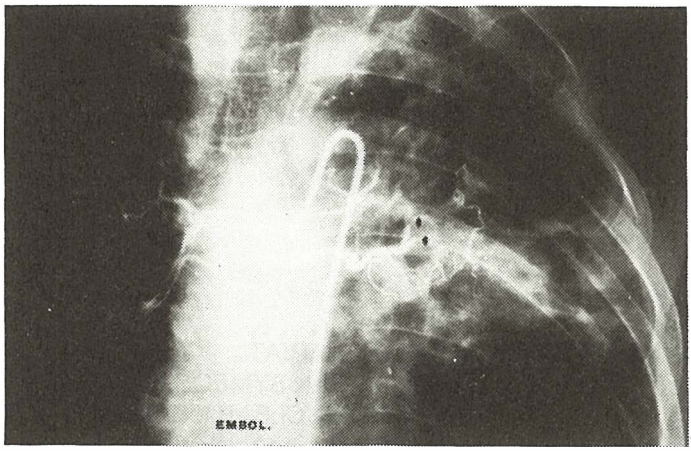

Figure 1b

(For answers see page 318)

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POSSIBILITIES OF COMPUTED TOMOGRAPHY IN EVALULATION OF GASTRIC NEOPLASMS EXTENSION

Jankulov V, Lincender L, Lovrinčević A, Obradov M

Abstract – During the period from January to December 1988, the computed tomography (CT) findings were evaluated in 30 patients with the diagnosis of neoplastic gastric process (double contrast X-ray imaging of the gastroduodenum and/or endoscopy).
The following parameters were evaluated: the gastric wall thickness exceeding 1 cm, infiltration of the surrounding structures, adenopathy, metastases in the parenchymal organs. The results show that the most frequent finding was wall thickness (70% of cases) infiltration (50%), adenopathy (30%), metastases (16,7%).
According to the results, it can be concluded that CT is not the primary diagnostic procedure in the gastric malignomas, but it can improve the »staging« and, suggest to the surgeons the resectability of the stomach.

UDC: 616.33-006.6–073.756.8

Key words: stomach neoplasms; tomography, x-ray computed

Orig sci paper

Radiol Iugosl 1991; 25:311-4.

Introduction – Gastric neopolasms are the most frequent the gastrointestinal tract tumors. Although the incidence of gastric tumors has been decreasing, especially in the USA, this disease presents a great health and social problem in our country (1). In some countries the incidence of this disease is extremely high (Japan, Chile, Island, Austria). In Japan, more than 50% of males affected by malignant diesease die of gastric malignoma (2). Members of the yellow race, males and the carriers of the blood group »A« have greater chances to develop gastric malignoma. The relation between males and females is 2:1 (2). The most frequent pathohistologic type is adenocarcinoma (95%), then lymphoma 3%) and leiomyosarcoma (2%) (2, 3). Introducing the computed tomography (CT) in the '70s, the primary interest of the clinicians focused on the evaluation of solid, parenchymatous abdominal organs. Relating to the level of CT technique development at that time, the information about the condition of digestive tract were inaccurate. Introducing the fast scanners with the technique of dynamic scanning, it was concluded that CT provides valuable data on extraluminal extension of gastric neoplasm (4, 5, 6, 7).

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Patients and methods – CT findings of 30 patients, obtained during the period from January to December 1988, were evaluated. Out of the primary diagnostic procedure in 9 patients, X-ray of gastroduodenum was applied in 13 patients and both diagnostic procedures in 8 patients. Of 17 patients who underwent endoscopy, pathohistologic finding was obtained in 14 patients. In the cases diagnosed by X-ray examinations of the stomach, we strictly followed the radiologic criteria for the diagnosis of gastric malignomas. The patients were prepared fot the examination in the same way as for X-ray of gastroduodenum; 600 ml of the diluted water-soluble contrast medium Telebrix 300 per os was administered. At the table, prior to the scanning the effervescent powder Visogas (Pliva)per os and Buscopan (2 mil i.v.) were applied. CT scans were obtained on either Somatom SF of Somatom DRH (Siemens), with 4-8 mm thick slices; the stomach was scanned from the level of esophagogastric junction to the level of pylorus.

The following parameters, showing the signs of neoplastic process, and its extragastric propagation were evaluated on the images:

– gastric wall thickness exceeding 1 cm,

– infiltration of perivisceral fat tissue and surrounding organs,
– adenopathy,
– metastases in the parenchymatous abdominal organs.

Results – Our series of 30 examined patients showed the greatest incidence of gastric malignomas in a group of male patients aged 51-60 years (Table 1 and 2); the rate of male VS. female patients is similar to the data from literature (2).

Table 3 shows the distribution of patients according to diagnostic procedures. Of the expected 17 pathohistologic findings, only 14 were obtained; there were 13 adenocarcinomas and one gastric lymphoma.

The most frequent finding on CT was gastric wall thickening exceeding 1 cm without signs of invasion of the surrounding structures, suggestive of tumor resectability (Table 4).

Table 1 – Sex distribution of patients

♂	19	63,4%
♀	11	36,6%

Table 2 – Age distribution according to groups

Age distribution	%
21 – 30	0
31 – 40	6,7
41 – 50	20
51 – 60	33,3
61 – 70	23,3
71 – 80	16,7

Table 3 – Distribution of patients according to diagnostic procedures

Diagnostic procedures	No of patients
Endoscopy	9
Endoscopy and X-ray of gastroduodenum	8
X-ray of gastroduodenum	13

Table 4 – Evaluated parameters

Wall thickness exceeding 1 cm	21/30 (70%)
Infiltration	15/30 (50%)
Adenopathy	9/30 (30%)
Metastases	5/30 (16,7%)

Discussion – In spite of the fact that the incidence of gastric malignomas has been decreasing in the developed as well as in our country (1, 2), this disease presents a serious problem from the point of early detection as well as therapy.

Till the introduction of endoscopy in the gastroenterological practice, the only method for diagnosis of gastric malignoma was X-ray of the stomach. Despite the relevant advances in the technique of investigation, early types of malignomas frequently remain undiagnosed. Our cases had two or more main radiologic signs of neoplasm.

Introducing fast CT scanners, radiologic diagnosis of gastric tumors has been significantly improved because of the possibility to evaluate the extraluminal progression of the process (4).

The most frequent change noticed in those conditions, confirmed also by our findings, was the decrease of wall thickness for more than 1 cm in the tumor area (4, 7) (Fig. 1a, 1b, 2a, 2b).

Besides this parameter, the signs of the surrounding organs invastion (6) Fig. 1c), adenopathy (4) (Fig. 1b), as well as the lesions in parenchymatous organs in the form of metastases (Fig. 2b) were noticed. During the evaluation of the examined group of patients, we did not search for the metastatic lesions outside the digestive system. The liver was evaluated as the primary site of neoplastic process disemination. For the optimal presentation of the stomach, the optimal preparation of the patient is neccessary, which is the »condition sine qua non« for an adequate analysis of the scans. CT of the stomach is not the primary diagnostic procedure in this group of patients, but it has the place in the algorithm of investigations. Other authors experiences are different; from those ignoring the possibilities of CT (8), to those who base the pathohistologic diagnosis on findings of this examination (5). According to our experience, based on the series of 30 patients, CT is the most adequate non-invasive method for »staging« of patients with gastric malignomas.

According to the American authors (6), patients are classified in three groups. The first group comprised patients without signs of surrounding structure invasion, who were candidates for surgery. The second group consisted of patients with signs of invasion and metastases, who would undergo palliative surgical interventions. In third group there were patients with undefined

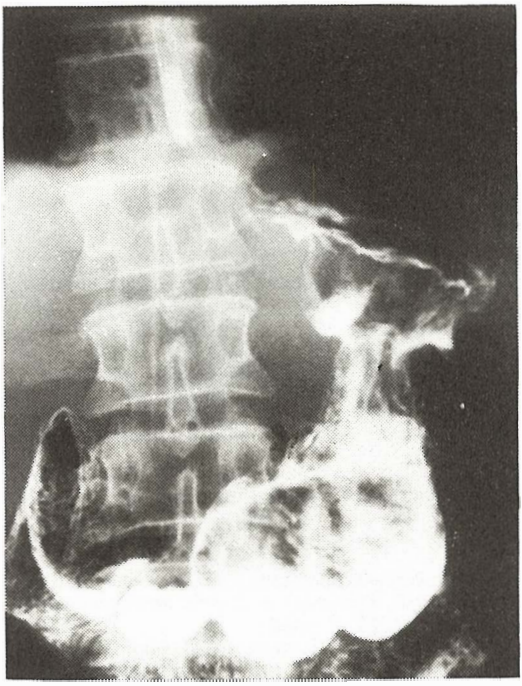

Fig. 1a – X-ray of gastroduodenum: subcardial infiltration of the stomach corpus

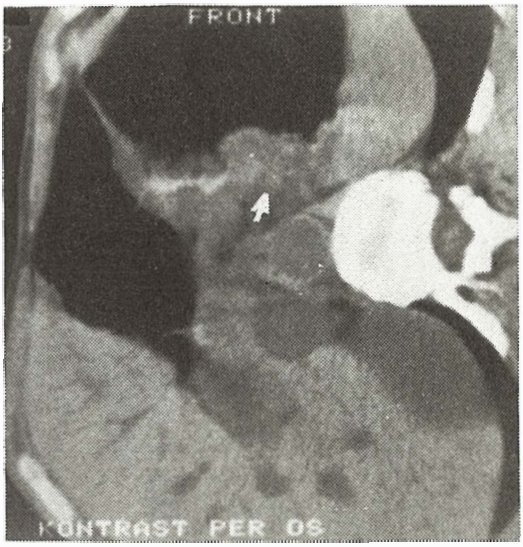

Fig. 1b – CT: wall thickness exceeding 1 cm, lymphnode enlargement in hepatogastric ligamment (arrow)

Fig. 1c – CT of the same patient three scans more caudally: the signs of retrogastric space infiltration

CT findings, who would undergo further diagnostic procedures. CT of the stomach has its plase also in surgically treated cases (8), although our experiences are too modest to form our own attitudes.

Conclusion – CT is not the primary diagnostic procedure in gastric malignomas, but on the basis of some parameters, disease staging and suggestions to the surgeon about resectability can be defined.

Adequate preparation of the patient and imaging conditions are neccessary for the analysis. At this level of CT development, pathohistologic diagnosis of gastric malignoma can not be defined.

Sažetak

MOGUĆNOSTI KOMPJUTORIZIRANE TOMOGRAFIJE U PROCJENI EKSTENZIJE NEOPLAZME ŽELUCA

U periodu od januara 1988. do decembra 1988. godine vršena je evaluacija CT nalaza kod 30 pacijenata sa postavljenom dijagnozom neoplastičnog procesa na želucu (rtg. gastroduodenuma sa dvostrukim kontrastnim sredstvom i/ili endoskopija).

Endoskopske i konvencionalne radiološke metode pregleda gastroduodenuma nam pružaju uvid u endoluminalni stepen ekstenzije procesa dok nam kompjuterska tomografija pruža odličan uvid u stepen ekstraluminalne ekstenzije u okolne strukture kao i postojanje metastatskih lezija. Uvođenjem CT-a olakšan je »staging« bolesnika kao i operativni plan.

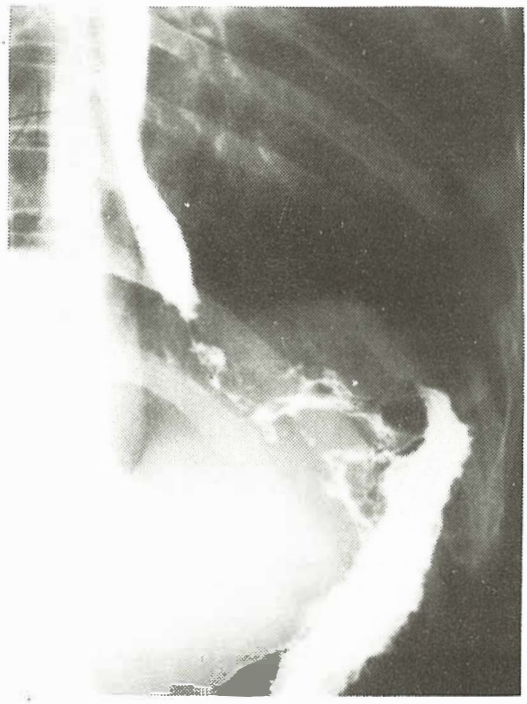

Fig. 2 – X-ray of gastroduodenum: infiltrative process of the cardia and fornix of the stomach

Cilj našeg rada je da odredi mjesto i ulogu kompjutorske tomografije kod bolesnika sa neoplazmom želuca.

References

1. Glavaš Ž, Dugalić D, Janković A, Parunović M, Jovanović R. Carcinoma ventriculi. U: Marković T. Stručno medicinski kriteriji za dijagnostiku i terapiju malignih tumora. Beograd: RSIZZZ, 1987: 137-50.

2. Kučišec A. Želudac. In: Piljac G. Rak (Klinička onkologija). Čakovec: TIZ »Zrinski«, 1977; 280-96.

3. Robbins LS. Stomach. In: Robbins LS, Cotran SR, Kumar V. Pathologic basis of disease. Philadelphia: W. B. Saunders Co., 1984: 806-27.

4. Balfe DM, Koehler RE, Karstaldt N, Stanley RJ, Sagel SS. Computed Tomography of gastric neoplasms. Radiology 1981; 140: 431-6.

Fig. 2b – CT (same patient): an expressed thickening of the gastric wall with metastases in the left liver lobe (arrow)

5. Bruneton JN, Caramella E, Cazenave P, Birtwisle Y, Hericord P, Drovillard J. Gastric leiomyosarcoma. Eur J Radiol 1987; 7:160-2.

6. Halversen RA, Thompson WM. Computed tomographic staging of gastrointestinal tract malignancies. Investigative Radiology 1987; 22:2-16.

7. Ćatić Dž. Kompjutorska tomografija digestivnog trakta. Doktorska disertacija, Sarajevo 1984; 1-162.

8. Sussman KS, Halvorsen RA Jr, Illescas FF et al. Gastric adenocarcinoma: CT versus surgical staging. Radiology 1988; 167:335-40.

9. Hammerman AM, Mirowitz SA, Susman N. The gastric air-fluid sign: Aid in CT assessment of gastric wall thickening. Gastrointest Radiol 1989; 14:109-12.

10. Lee KR, Levine F, Moffrat RE, Bigongiari LR, Hermreck AS. Computed tomographic staging of malignant gastric neoplasm. Radiology 1979; 133:151-5.

11. Balfe DM, Mauro MA, Koehler RE, et al. Gastrohepatic ligament. Normal and pathologic CT anatomy. Radiology 1984; 150:485-90.

12. Komaiko MS. Gastric neoplasm: Ultrasound and CT evaluation. Gastrointest. Radiol 1979; 4:131-7.

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UNIVERSITY HOSPITAL »DR O. NOVOSEL« ZAGREB

APPLICATION OF INTRAOPERATIVE ULTRASONOGRAPHY IN BILIARY SURGERY

Drinković I, Gabelica V, Makaruha B, Župančić K, Boko H, Brkljačić B, Vidjak V

Abstract – In surgical practice billiary tract diseases are quite common. A whole range of preoperative diagnostic procedures has been developed in order to discover them: ultrasonography, cholangilography, retrograde cholangiography, computed tomography and magnetic resonance imaging.
Despite of their high accuracy, obstructive icterus in many patients still remains of vague genesis.
With 57 patients, suspected to have jaundice caused by choledocholithiasis or suspected to have choledocholithiasis, intraoperative sonography proved satisfactory in 90% of patients.
The accuracy of the findings, absence of radiological exposure and the opportunity to plan surgical treatment are advantages of this technique.

UDC: 616.361-089:616.361-073:534-8

Key words: biliary surgery; ultrasonography, intraoperative period

Orig sci paper

Radiol Iugosl 1991; 25:315-7.

Introduction – In biliary surgery, intraoperative ultrasonography is believed to be one of the most important diagnostic imaging methods in an adequate surgical treatment of hepatic and biliar tract diseases. By additional improvement of machines, the accuracy of intraoperative ultrasonography in detecting biliary tract diseases has highly increased. Surgeons are provided with a safe, accurate and less invastive method for discovering and localization of common bile duct diseases. In our surgical practice a whole range of diagnostic procedures has been used: intraoperative cholangiography, cholangiomanometry and choledoscopy.

During the last seven years, intraoperative ultrasonography has been applied as a method which enables direct visualization of biliary tree and choledochus.

Material and methods – In our surgical practice during the last four years, intraoperative ultrasonography was carried out in 57 patients suspected of having choledocholithiasis. At the same time, examination results were checked by using intraoperative cholangiography through the resected cystic duct.

For that purpose we have been using a special ultrasonic machine, type Scanel 300, with image memory, linear 7 MHz probe, dimension 4x1x1 cm, and focal distance of 2.5 cm. It enables a valuable ultrasonic imaging of the liver and the common bile duct. Mechanically well cleaned, non-sterile probe is placed into a disposable sterile plastic bag before being used by the surgeon directly in the operative field. Transmission cable is put into a sterile linen cover. The sterile plstic bag has to be filled with paraffine oil in advance in order to achieve valuable conductivity of US signal. In order to improve the acoustic contact, a warm (37°) physiological Na Cl) solution is introduced into the operative field.

The probe is placed under the tissue to be scanned, approximately 0.5 to 1.5 cm away from the surface of structures. Compression of the scanned structures by the probe is not allowed, because clear visualization of the surface of the tissue could be lost. In our surgical practice we have usually been using the right subcostal section to reach the common bile duct before ultrasound examination is performed. Gallbladder is scanned from fundus via istmus to the mouth of the cystic duct into the common bile duct. The common bile duct should be examined

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by both longitudinal scanning and transverse scanning. Papila Vateri should also be examined.

After extensive mobilization of the duodenum according to Kocher's method is performed, we start examining the retropancreatic part of the bile duct and papila vateri. Furthermore, we measured the diameter of the common bile duct and thickness of the wall and examined a possible presence of pathological masses or neoplastic lesions in the common bile duct. We identified the anatomic relationship between the common bile duct and the surrounding big vessels.

Our next step will be determined by the examination results.

Results – Intraoperative US and intraoperative cholangiography were performed in 57 cases with suspected choledocholithiasis or obstructive jaundice.

In 37 cases both methods indicated choledocholithiasis. In 20 cases choledocholithiasis was not confirmed by any of the methods, or we found other benign or malignant lesions. Among 37 patients with positive findins, US and colangiography indicated the same result in 33 patients. In 4 patients the results were different.

With 3 patients the cholangiographic examination was positive and the US examination was negative. In one case the US examination was positive and the cholangiographic examination was negative.

After surgical treatment, we obtained the following results: cholangiography was false positive in three patients, false negative in two patients (true positive 34 patients, true negative 22 patients). US was false positive in one patient, and false negative in one patient (true positive 36 patients, true negative 21 patients).

By cholangiographic examination, sensitivity was 94%, specifity 88% and accuracy 91%.

By US examination, sensitivity was 97%, specifity 95% and accuracy 96%.

Discussion – Intraoperative ultrasonography is a relatively simple technique and provides surgeons with a number of valuable information. Besides, the use of ultrasonography in surgery avoids exposing the patient and the surgical team to radiation, which seems to be inevitable during intraoperative radiological examinations.

Furthermore, the possibility of an allergic reaction to a contrast material is highly reduced.

Considering the time duration, the application of ultrasonography in biliary surgery is unlimited and can be repeated several times in the course

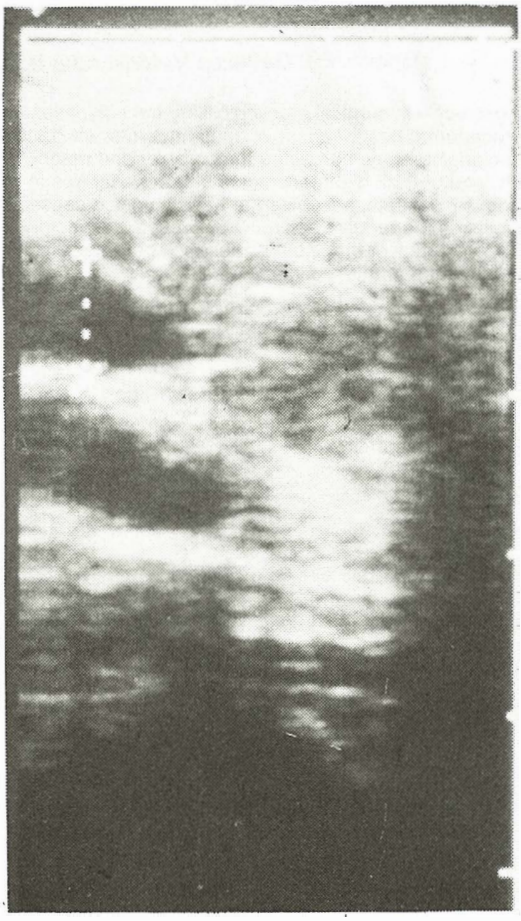

Fig. 1 – Choledochus and lumen stricture caused by tumor

of operation. It enables an insight into the caliber of common bile duct and the demonstration of the relation of biliary duct to surrounding organs, especially to the vascular ones. Further advantages include more image information on cancer masses and their metastases (Figure 1). Considering the choice of surgical methods, this kind of examination will provide us with more optimal decisions. According to the data from (secondary) literature, the exactly performed intraoperative biliary ultrasonography in detecting biliary calculi, especially within the lumen of the common bile duct, proved to be satisfactory with over 96% of patients (1-8).

Therefore the high accuracy of intraoperative ultrasonography proved to be more advantageous than intraoperative radiological methods, especially in discovering small calculi (Figure 2).

Fig. 2 – Small calculi in choledochus (size 2 to 3 mm)

Our experience with intraoperative ultrasonography in biliary surgery has enabled us to define intraoperative radiographic cholangiography as a complementary method in the case we miss relevant information.

Conclusions – Based on the results of our clinical experience, we conclude that application of ultrasonography in biliary surgery is a new contribution to the intraoperative localization of common bile duct calculi. Furthermore, intraoperative ultrasonography provides biliary surgeons with a new, safer and more accurate screening procedure for common duct calculi.

References

1. Sigel B, Coelho JC, Spigos DG, Donahue PE, Wood DK, Nyhus LM. Ultrasonic imaging during biliary and pancreatic surgery. Am J Surg, 1981; 141:84-9.

2. Rifkin MD, Rosato FE, Branch HM, Foster J, Shuin-Lin Yang, Barbot DJ, Marks GJ. Intraoperative ultrasound of the liver. Ann Surg 1987; 205(5%:466-72.

3. Chardavoyne R, Kumary-Subhaya S, Auguste LJ, Philips G, Stein TA, Wise L. Comparasion of intraoperative ultrasonography and cholangiography in detection of small common bile duct stenos. Ann Surg 1987; 206(1):53-5.

4. Jakomowicz JJ, Rutten H, Jurgens PJ, Carol EL. Comparasion of operative ultrasonography and the radiography in screening of the common bile duct. World J Surg 1987; 11(5):628-34.

5. Klotter HJ, Rockert K, Kummerle P, Rothmund M. The use of intraoperative sonography in endocrine tumors of the pancreas. World J Surg 1987; 11(5):634-41.

6. Sigel B, Machi J, Kikuchi T, Anderson KW, Horrow M, Zaren HA. The use of ultrasound during surgery for complications of pancreatitis. World Surg 1987; 11 (5):659-63.

7. Štulhofer M. et al. Intraoperativna ultrasonografija hepatoholedohusa. Digestivna kirurgija 1985; 361.

8. Yiengpruksawan A, Genepola P. Extended applications of ultrasonography by the surgeon. Am J Surg, 1987; 153:221-5.

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FROM PRACTICE FOR PRACTICE

CARIDIOVASCULAR SYSTEM

Case 4

Answer: This is a selective bronchial arteriogram which shows multiple abnormal vessels in the left upper zone. In the midst of these vessels is an area of density which represents extravasa contrast medium which indicates active Bleeding from the Bronchial Artery. The bronchial bleeding is likely to be arising in an area of bronchiectasis or scarring left by the patients previous tuberculosis.

This type of bleeding is difficult to control and requires either surgical or radiological treatment. In that case the patient had very poor respiratory function and was not fit for thoracotomy. The bleeding artery was embolized with immediate control of the haemorrhage and rapid and sustained recovery. Severe bronchial artery bleeding of this type can also complicate bronchiectasis (particulary complicating cystic fibrosis), carcinoma, micetoma, pulmonary abscess, idiopathic pulmonary haemorrhage and various other chronic fibritic lung diseases and is often amenable to treatment by embolization (Figure 1b).

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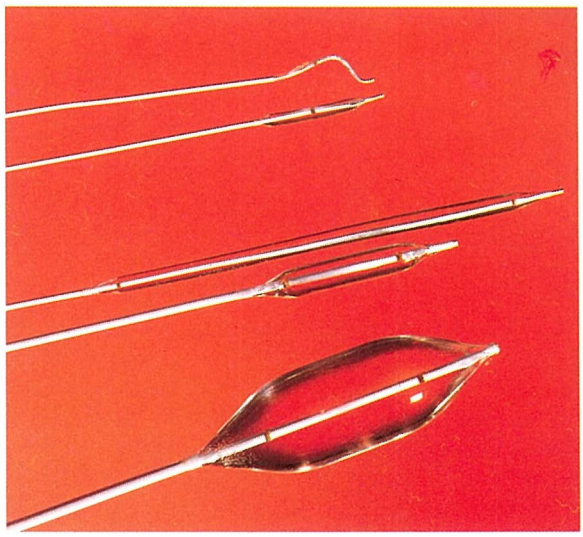

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VALUES OF TSH RECEPTOR AUTOANTIBODIES (TRAb) IN PATIENTS WITH TREATED GRAVES' DISEASE

Paunković N, Paunković J, Pavlović O

Abstract – Serum levels of TRAb, thyroid hormones and thyrotropin and clinical status were investigated in 114 patients with treated Graves disease. The following results were obtained: of 66 patients treated with methimazole (follow-up 18 months during treatment and 12 months after), 47 had normalized values of TRAb and thyroid hormones and eumetabolic clinical state. After 6 to 10 months 7 of them developed relapse of disease. In 19 with persistently high TRAb levels under treatment, 12 were continously hyperthyroid (in all of them relapse occured up to 3 months after cessation of treatment) and 7 patients had periodical episodes of hypothyroidism.
Of 25 patients treated with radioiodine 1 to 12 years ago, TRAb levels normalized in 20 (17 euthyroid, 3 hypothyroid), and remained elevated in 5 (4 hyperthyroid and 1 hypothyroid) during 1-2 years after treatment. Of 23 surgically treated patients TRAb serum levels normalized in 16 (6 euthyroid, 1 hyperthyroid) for 12-24 months. These findings support observations on TRAb significance in pathogenesis and evolution of Graves' disease.

UDC: 616.441-008.61-074

Key words: Graves' disease; autoantibodies; receptors, thyrotropin

Orig sci paper

Radiol Iugosl 1991; 25:319-23.

Introduction – Thyrotropin receptor autoantibodies (TRAb) are the most frequent thyroid stimulatory immunoglobulins (TSI, TSAb) although they (TSAb) sometimes coexist with thyroid-blocking antibodies (TSBAb) or change into them during hyperthyroidism (1-4). Treatment of Graves' disease (antithyroid drugs, thyroidectomy, radioactive iodine) should influence TRAb circulatory levels (5,6).

Follow-up of TRAb in 114 treated patients and comparison of findings with thyroid hormone levels and clinical status are presented.

Patients and methods – The investigation was conducted in 114 patients with Graves' disease divided into three groups, based on type of treatment. Group I consisted of 66 patients treated with methimazole (Favistan, Bosnalijek). Duration of treatment was 18–21 months. Starting dose was usualy 60 mg daily and was diminished during treatment according to metabolic state of patient. Thyroid hormones were not added. Follow-up of patients was performed during the whole treatment and at least months after that. Group II consisted of 25 patients treated with radioactive iodine (131-I). Therapeutic dose was applied once in 16 patients, twice in 8 and three times in 1 patient). In 9 patients of this group, follow-up was performed from the application of radioactive iodine up to 12 to 60 months. In 16 patients check up was performed only once (last application of radioiodine was more than 5 years ago). Group III consisted of 23 patients with bilateral subtotal thyroidectomy. In 11 patients follow-up began right after surgery and lasted 12 to 36 months, while in 12 patients check up was done only once (patients operated on more than five years ago.)

Thyroid metabolic status of patients was evaluated by two independent experienced endocrinologists. Serum levels of thyroid hormones were determined by routine RIA, and receptor-TSH autoantibodies were determined by radioreceptor assay (TRAK-assay, Henning).

Results – The obtained results are presented in Tables 1, 2 and 3. Serum levels of TRAb in follow-up studies are indicated by arrows: with decreasing magnitude to normalization, or continously elevated in patients with permanent high TRAb. Results are illustrated in four cases (2 treated with methimazole and 2 surgically) (graph 1-4).

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Table 1 – Graves' disease, 66 patients, methimazole
follow – up during treatment (18–21 months) and at least 6 months after cesation

TRAb	↓	↑	total
n	47	19	66
issue	eu 47	hiper hypo trans 12 7	total 66
relapse	7	12 3	22

Table 2 – Graves' disease, 25 patients, ^{131}I therapy
follow – up (12 – 60 months)

TRAb	↓	↑	total
n	5	4	9
issue	eu 4	hypo 1	hyper (12 months) 4	total 9

Testing in remission (over 5 years)

TRAb	normal	high	total
n	15	1	16
issue	eu 13	hypo 2	hypo 1	total 16

Table 3 – Graves' disease, 23 operated patients
follow – up (12 – 36 months)

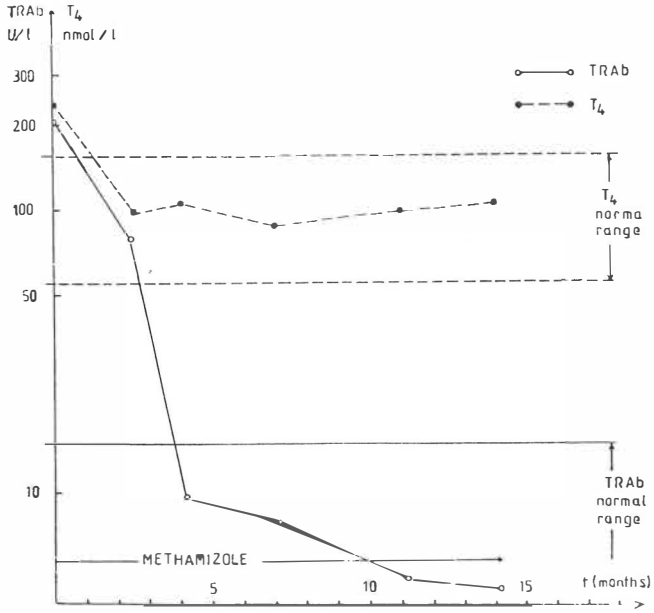
TRAb	↓	↑	total
n	5	6	11
issue	eu 4	hypo 1	eu 5	hyper 1	total 11

Testing in remision (over 5 years)

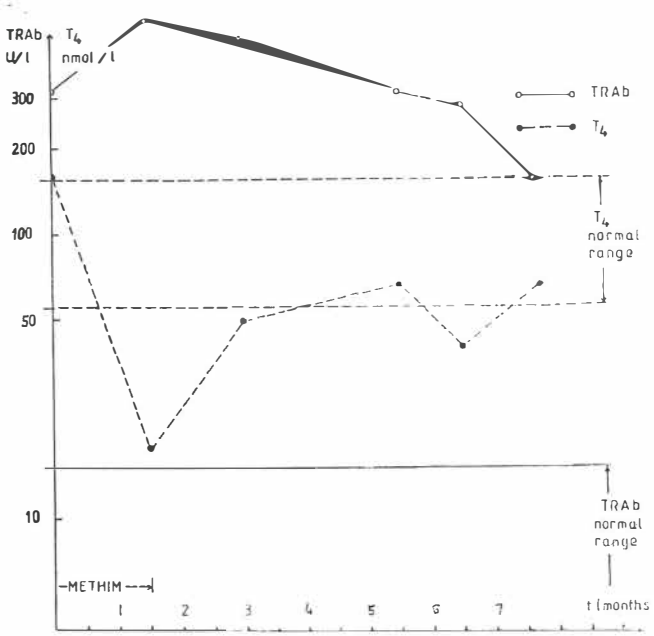
TRAb	normal	high	total
n	11	1	12
issue	eu 8	hypo 3	eu 1	total 12

Discussion – Of 66 patients treated with methimazole more than 70% (47 patients) were good responders (reestablishment of remission, TRAb normalization). These findings are slightly better than some recently reported data (7). There is an attractive hypothesis that methimazole has an immunosupressive effect which results in diminished TRAb serum levels and consequent normalization of thyroid metabolic and hormonal state (4,8). It should also be considered that TRAb normalization could be a consequence of decrease in thyroid hormones levels as a result of direct thyrostatic action of methimazole (9). In 12 patients in spite of high doses of methimazole hyperthyroidism was persistent with elevated TRAb levels (nonresponders). In 7 patients despite high TRAb concentrations, transitory hypothyroidism was observed. We have not tested TRAb activity by postreceptor effects (cAMP generation), but we assume that the high TRAb concentrations accompanying hypothyroidism point out their thyroblocking effect (4.10).

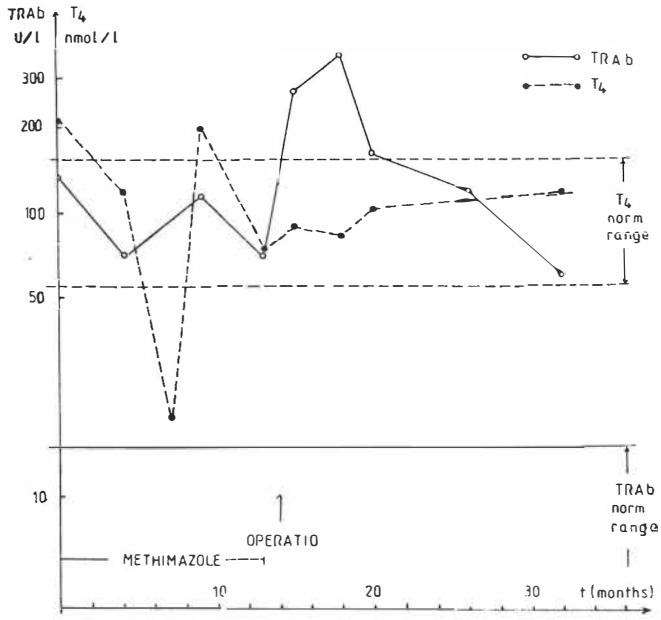
Patients with persistently elevated TRAb levels, several months after 131-I therapy, remained hyperthyroid (all of them required additional therapeutic dose). Patients in longer remission after radioiodine therapy had normal TRAb levels. These findings are not in accordance with



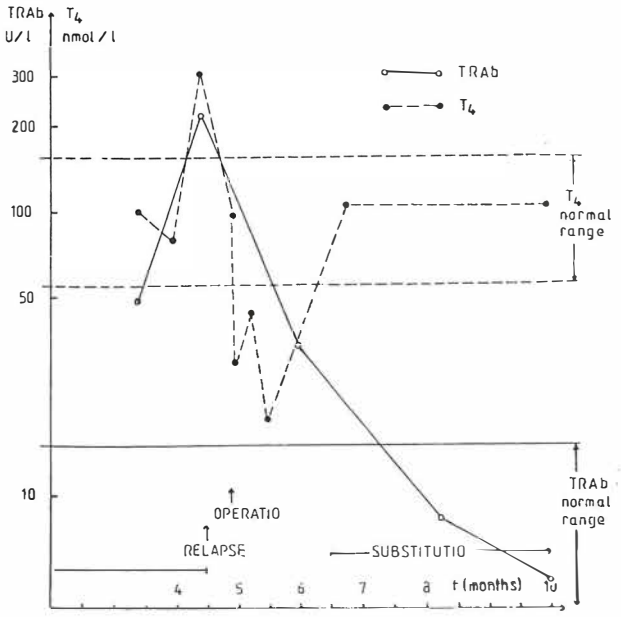
Graph 1 – Case report: concordant normalization of T_4 and TRAb under mathimazole treatment



Graph 2 – Case report: persistence of high TRAb levels and low T_4 after a short methimasole therapy (TBAb?)



Graph 3 – Case report: persistence of TRAb few months after subtotal thyroidectomy with euthyroidism



Graph 4 – Case report: early postoperative hypothyroidism and rapid TRAb decrease

some reports in which patients in remission exhibit high TRAb levels (11), but are similar to others (12). Low incidence of hypothyroidism in our group of treated patients is probably due to application of low doses of 131-I (3MBq/g). These low doses have effect on the lymphocytes of the thyroid responsible for TRAb production, and have not enormous thyreonecrotic effect.(13).

After bilateral subtotal thyreoidectomy, functional thyroid status is normalized prior to TRAb levels (in 6 of 11 patients in early follow-up study). In one patient with early postoperative hypothyroidism rapid TRAb decrease was registrated. Patients in longer remission had normal TRAb levels.

Our results support opinions that TRAb (TSAb) have important role in pathogenesis of immunogenic hyperthyroidism. However, some observations must be supplemented by following investigations (distinguishing thyrostimualting from thyroblocking antibodies) or by testing some immunologic factors other than TRAb (thyroid microsomal antibodies etc).

References

1. McKenzie JM, Zakarija M, Sato A. Humoral immunity in Graves' disease. Clin Endocrinol Metab 1978; 7:31-46.

2. Orgiazzi J, Madec AM. Le recepteur de la TSH. Annales d'Endocrinologie (Paris) 1989; 50:418-24.

3. Endo K, Kasaga T, Konishi J et al. Detection and properties of TSH-binding inhibitor immunoglobulins in patients with Graves' disease and Hashimoto-s thyroiditis. J Clin Endocirnol Metab 1978; 46:734-39.

4. Fenzi GF, Hashizume K, Roudebush CB, DeGroot LJ. Changes in thyroid stimulating immunoglobulin during antithyroid therapy. J Clin Endocrinol Metab 1979; 48:572-6.

5. Rapaport B, Greenspan S, Foletti S, Pepitone M. Clinical experience with a human thyroid cell bioassay for thyroid stimulating immunoglobulin. J Clin Endocrinol Metab 1984; 58:332-8.

6. McGregor AM, Peterson MM, Capiferri R et al. Effects of radioiodine on thyrotropin-binding inhibitory immunoglobulins in Graves' disease. Clin Endocrinol 1079; 11:437-44.

7. Budihna N, Pavlin K. TSH-receptor antibodies in the sera of patients with immunogenic hypethyroidism (Graves' disease) during antithyroid therapy. Eur Nucl Med Congress, Goslar, 1986.

8. McGregor AM, Ress–Smith B, Hall R. Specificity of the immunosupresive action of carbimazole in Graves' disease. Brit. Med J 1982; 284:1750-1.

9. Volpe R. Immunoregulation in autoimmune thyroid disease. N Eng J Med 1987;316:44-6.

10. Botger IG, Pabst HW. Clinical value of TSH receptor autoantibodies (TRAb) by radioreceptorassay (RRA). Eur Nucl Med Congress, London, 1985.

11. Marana G, Marin MC, Haro J et al. TSH receptor autoantibody measurement in clinical; evolution of thyrotoxicosis. Ibidem.

12. Kozak B, Lauterbach W, Ledda R et al. Sonographic patterns and TSH-receptor autoantibody titers in immunogenic and non-immunogenic thyrotoxicosis before and after radioiodine therapy. Ibidem.

13. Goolden AWG. Treatment of hyperthyroidism with radioiodine. IV jugoslovenski kongres nuklearne medicine, Beograd, 1986.

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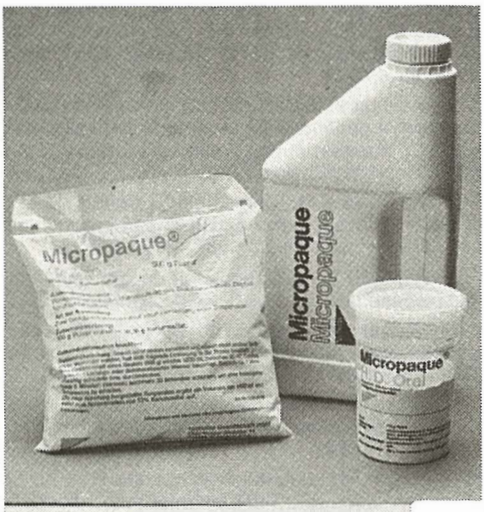

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PRELIMINARY REPORT ON RADIOCHEMICAL AND PRECLINICAL STUDY FOR THE REGISTRATION OF SCINTIMUN CEA IN HUNGARY

Rakiás F[1], Szentgyörgy P[1], Jánoki Gy[2]

Abstract – The radiochemical purity of Scintimun CEA was determined by rapid chromatographic method on ITLC Gelman SG layers. Three types of developing solution were used: methylethylketone, 0,9% (isotonic) sodium chloride solution and sodium carbonate solution of 3 mol/l concentration. The most significant results were obtained by developing with the sodium carbonate solution. In this case the distribution of the radioactivity along the chromatographic layers indicated that about 94% of the total amount of the labelling Tc was found at the start point (as bound to Mab), 3% migrated together with the front of the developing solution (free pertechnetate ions as radiochemical impurity). The remaining 3% were distributed along the chromatographic layer (as other bound radioactive impurities). The stability tests of the labelled solution were performed after 3 hours. No significant differencies could be evidenced by these measurements. The preclinical testing consisted of the activity distribution measuerements between different mouse organs including malignant tumour. It has been shown that the best distribution time is 24 hours after the administration of the diagnostics.

UDC: 616-006.6-097

Key words: carcinoembryonic antigen; antibodies, monoclonal; technetium, radiochemical purity, radiopharmaceuticals, diagnostics, distribution in organs, malignant tumour

Orig sci paper

Radiol Iugosl 1991; 25:325-9.

Introduction – A large number of monoclonal antibodies labelled with different radionuclides such as 131-I, 111-In, 125-I have been described in the litereture for scintigraphic diagnosis of cancerous tumours (1–8). A relatively new one is the medicinal product SCINTIMUN CEA (monoclonal Carcino-Embryonic Antigen) produced by Behring-Werke, F.R. Germany, labelled with ^{99m}Tc. We have examined such kits for registration purpose. Radiochemical purity examinations and preclinical tests were carried out to prove the diagnosis.

Materials and methods – All reagents used for ITL chromatography were of analytical grade.

The biological tests were made with five groups of four DBA respectively CBA mice. The immunsuppression was achieved as follows: the thymus of mice aged 3–4 weeks was extirped. A week later the mice were irradiated with gamma rays (8.5 Gy per whole body), followed by bone marrow transplantation. After another week human tumour was xenografted. The biological tests referring to the technetium distribution in various mouse organs were made 2–3 weeks after an injection of the labelled (22–44 MBq) antibody (0.04--0,08mg).

^{99m}Tc labelling of SCINTIMUN CEA – The kit to be examined consisted of two sterile vials. One of them contained the lyophilized monoclonal antibody 431/26 (the active component) together with sodium phosphate (buffering agent) and D-Glucitol (anticoagulant). The content of the other vial was the following: tin (II) chloride dihadrate (for reducing pertechnetate ions to technetium ions), tetrasodium 1,1,3,3, propane-tetraphosphonate dihidrate (PTP, complexing agent) and sodium chloride (agent to form isotonic solution).

The active component of the kit was lebelled with ^{99m}Tc eluated from the technetium generator AMERTEC II, supplied by Amersham International England. The labelling was performed according to the directions for use. Five ml of isotonic sodium chloride solution was introduced by a syringe into the vial containing the tin(II) chloride. After dissolving the dry substance contained in this vial, one ml of the obtained solution was injected into the vial which contained the monoclonal antibody, dissolving the dry content in the vial. By interaction mainly between the antibody and the tetrasodium 1,1,3,3, propane-phosphonate, reactive sites have been created for complexing metal ions such as technetium(IV). An

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adequate aliquot of technetium generator eluate containing pertechnetate ions of 540 – 1230 MBq activity was added to the previously obtained solution. Tin chloride reduced the pertechnetate ions to technetium ions making in this way possible its linking by ligand bonds to the reactive sites of the antibody. Waiting for ten minutes, the monoclonal antibody 431/26 has been labelled with ^{99m}Tc. This solution was diluted with isotonic sodium chloride solution to obtain labelled solution of 15–20 MBq/ml specific activity, allowed to thin layer chromatographic radiochemical purity testing.

Testing of labelled SCINTIMUN for radiochemical purity – Thin layer chromatography was performed according to the registration protocol (9,10) using Gelman SG layers and methylethylketone, isotonic sodium chloride and 3 mol/l sodium carbonate as developing solutions. We used three chromatographic layers for testing the monoclonal antibody and one for the technetium standard solution.

Three sets of chromatographic layers containing each four layers were preparad to develop them in three different developing solutions. After drying, the sets of layers were placed into three different chromatographic vessels. To saturate the atmosphere, the developing solutions were introduced 24 hours before into the corresponding vessel. The developing times were 15 m for both methylethylketone and isotonic sodium chloride solution; and 60 m for the sodium carbonate solution of 3 mol/l concentration.

Two series of examination were made. The first one was made 10 minutes after the introduction of labelling technetium eluate into the vial which contained the activated antibody. The second one, i.e. the stability examination was performed 3 hours after the labelling procedure.

Measuring device – For the measurement of gamma-activity of technetium radionuclide the computer controlled Auto-Gamma Counting System COBRA of PACKARD INSTRUMENT COMPANY (USA) Model 5005 was used. The measured data were registered in a protocol of the Cobra system, as well on a magnetic floppy disk. The registered data were processed by a program written by us based on the facilities of commonly used software package, either by the computer of the Cobra System or by another computer. In this way it was possible to use the Cobra System mainly for activity measurements and to create portable data files.

Evaluation – Processing the measured data by a program written for this purpose, there were chromatograms of the labelled Scintimun CEA and of the technetium standard constructed. The mean values of the front middle and start activities together with the reliability limits of the means, were computed taking acount of the Student's repartition law of the errors, for reliability level of 0.05.

The interpretation of the chromatograms was performed according to the indications given in the registration documentation (9,10).

Results –The activity distribution of the labelling technetium along the chromatographic layers indicated that developing by methylethylketone and isotonic sodium chloride solutions, the active component of the diagnostics, the labelled monoclonal antibody was not separated from the other components of the samples (D-Glucitol, PTP, reduced-hydrolyzed technetium, free technetate).

Better results were obtained developing the chromatograms by sodium carbonate solution of 3 mol/l concentration. In this case the activity of the start place is due only to the labelled antibody. The other components of the samples were found in the chromatographic front (Fig. 1).

From the data table computed and organized by our data processing program, we present some extraction in Table 1.

The start, middle and front activity domains on the chromatographic layers were determined from the measured counting rates and from the graphs constructed by the computer programe. The influence of marking the limits for these domains is shown in table 1, sample number 1S. There were no differences concerning the activity distributions of the main component (Mab) of the samples. Differences could be only for the distributions of various impurity components. No differences could be noticed neither for examinations made after labelling (samples 1,2,3) nor for stability measurements (samples 1S,2S,3S). The Mab content of all samples exceeded the prescribed value of 70% given in the registration documents of Scintimun (10).

According to the facts presented above, we concluded that by radiochemical purity examinations of Scintimun CEA samples, the separation of the active component (Mab) from various impurities can be carried out using for developing only the sodium carbonate solution.

The preclinical examination of Scintimun consisted of the radioactivity distribution measu-

Table 1 – The activity distribution for labelled scintimun CEA

Developing solution	sample no.	start act. mab %	middle act. %	front act. free Tc + glucitol + PTP %
	1	75.6±0.8	7.8 ± 1.9	16.6 ± 2.0
	2	94.4 ± 0.6	3.2 ± 0.9	2.4 ± 0.2
Na_2CO_3	3	90.2 ± 1.7	6.4 ± 1.5	3.4 ± 0.4
3 mol/l	1S	84.1 ± 1.7	13.1 ± 5.4	2.8 ± 4.8
		86.3 ± 1.3	1.6 ± 0.7	12.4 ± 0.8
solution	2S	95.2 ± 0.2	2.9 ± 0.3	1.9 ± 0.1
	3S	91.7 ± 1.3	6.6 ± 1.4	1.6 ± 0.4

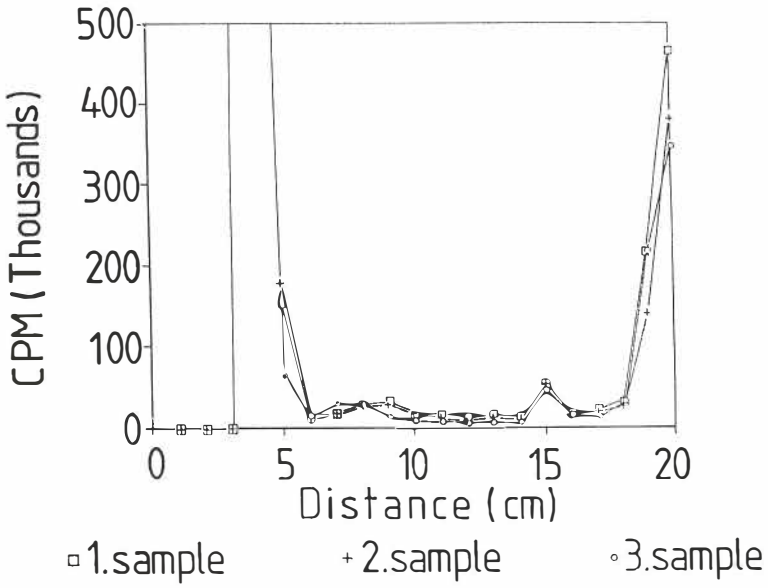


Fig 1 – The chromatogram of the labelled scinitimun CEA developed with sodium carbonate solution of 3 mol/l concentration.

rements in different mouse organs, it different time elapsed after the administration of diagnostics. Figure 2 shows the distribution of the labelling technetium among different organs twenty four hour hours after the administration.

Fig. 3 represents the technetium content of the tumour after various time has elapsed since the time of administration.

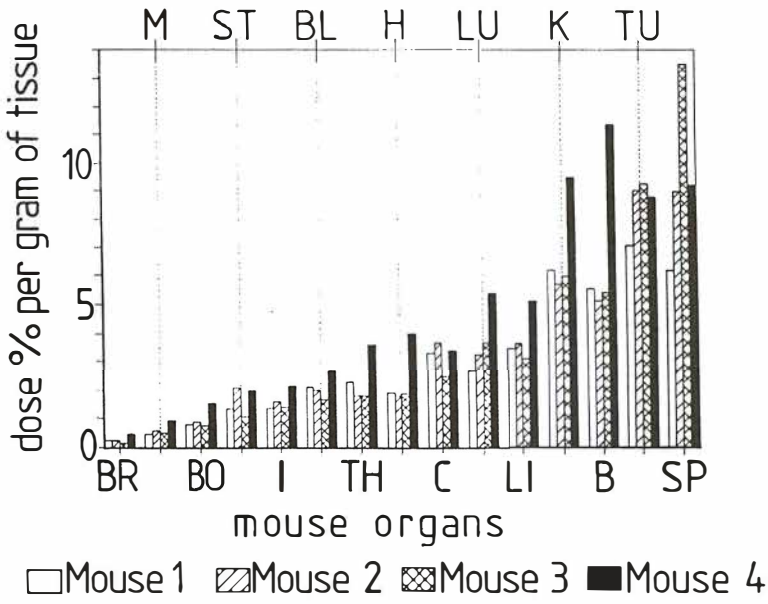
Conclusions – Among the working methods described in the registration documentation of Scintimun CEA for radiochemical purity testings, the method which uses sodium carbonate of 3 mol/l concentration as a developing solution of the chromatograms gave the best results. We suggest to use only this method for quick routine quality examinations.

2. The examined three samples originating from different production lots satisfied the quality requirements for radiochemical purity.

3. The distribution of the technetium among various mouse organs indicated that the best distribution time was 24 hours after diagnostic administration.

References

1. Amersham International, Nuclear Medicine Catalogue, 1990
2. Bares R, Fass J, Troung S, Buell U, Schumpelick V. Clinical Impact of Immunoscintigraphy for Diagnosis



TU	– tumour	BO	– bone	SP	– spleen
B	– blood	K	– kidney	ST	– stomach
LI	– liver	I	– intestine	BL	– bladder
M	– muscle	BR	– brain	H	– heart
C	– colon	LU	– lung	TH	– thyroid

Fig. 2 – The activity distribution among various mouse organs.

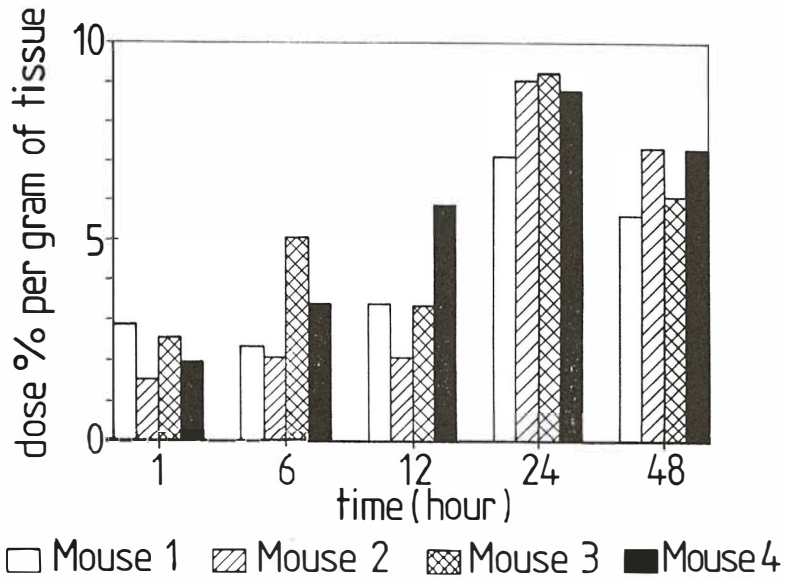


Fig. 3 – The activity of the tumour vs. time after injection.

and Therapy of Colorectal Cancer Evaluated after 1–Year Follow-up. European Nuclear Medicine Congress 1990, Amsterdam, Schattauer, Stuttgart-New York, 1991, 366.

3. Aronsson EF, Gretarsdottir J, Jacobsson L, Mattsson S, Holmberg SB, Hafstrom LO, Karlsson B, Lindholm. Comparison of Seven Iodine-Labelled Monoclonal Antibodies in Nude Mice with Human Colon Carcinoma Xenografts. Acta Oncol, 1991; 30:385-93. 30:385-93.

4. Lind P, Lechner P, Arianschad K, Klimplfinger M, Cesnik H, Kammerhuber F, Eber O. Anti-Carcinoembryonic Antigen Immunoscintigraphy (Technetium-99m-Monoclonal Antibody Bw 431/26) and Serum CEA Levels in Patients with Suspected Primary and Recurrent Colorectal Carcinoma. J Nucl Med 1991; 32:1319-25.

5. Granowska M, Mather SJ, Britton KE. Diagnostic Evaluation of In-111 and 99m Tc Radiolabelled Monoclonal Antibodies in Ovarian and Colorectal Cancer – Correlations with Surgery. Nuclear Medicine and Biology International Journal of Radiation Applications and Instrumentation Part B. 1991; 18:413-24.

6. Sheldon K, Reilly R, Baumal R, Marks A. Imaging of Human Ovarian Tumour Xenografts in Nude Mice Using Novel In-111-Labelled Monoclonal Antibody (10B). Nuclear Medicine and Biology–International Journal of Radiation Applications and Instrumentation Part B. 1991; 10:519-26.

7. Davidson BR, Waddington WA, Short MD, Boulos PB. Intraoperative Localization of Colorectal Cancers Using Radiolabelled Monoclonal Antibodies. BJ Surg 1991; 78:664-70.

8. Lamki LM, Buzdar Au, Singletary SE, Rosenblum MG, Bhadkamkar V, Espoarza L, Podoloff DA, Zukiwski A, Hortobagyi GN, Murray JL. Indium-111-Labelled B72.3 Monoclonal Antibody in the Detection and Staging of Breast Cancer – A Phase-I Study. J Nucl Med 1991; 32:1326-32.

9. Scintimun documentation, Part II., 3:1065.

10. Scintimun documentation, Part I., 1:25.

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PEDIATRIC CLINIC AND POLYCLINIC »PROF DR M. SARVAN« SARAJEVO

GFR (Cr-EDTA) VALUES IN CHILDREN WITH IDDM WITH RESPECT TO THE DISEASE DURATION

Grujić E, Dučić V, Babović D, Arifhodžić N

Abstract – The aim of the work has been to investigate the extent of the presence of renal dysfunction in insulin dependent diabetic patients by glomerular filtration rate evaluation using Cr-EDTA method. Mean GFR in diabetic children during the first year of the disease is 186.18 ml/min/1,73m2, when 65.27% diabetic children had an elevated GFR. During 3-5 year diabetes duration mean GFR was 176.52 ml/min/1.73m2 and 41.67% children had had elevated GFR. With the duration of the disease 6-10 years, mean GFR was 139.17 ml/min/1.73m2, but 39,13% diabetic children had elevated GFR.

UDC: 616.379-008.64:616.61-072.7

Key words: diabetes mellitus, insulin-dependent; glomerular filtration rate; chromium

Profess paper

Radiol Iugosl 1991; 25:331-4.

Introduction – Symptoms of disturbances in renal functions such as elevated glomerular filtration, increased urinary excretion of albumine and nephromegalia, are also present at the time of insulin-dependent diabetes diagnosis establishment.

After stabilisation of the diseases, in a majority of patients, the symptoms either disappear or remain in the subclinical stage for a long period of time. After 10-15 years of diabetes, the symptoms of diabetic nephropathy become manifest first in the incipient form to turn into clinically manifest nephropathy later on.

Mogesen et al. (1) have devided the course of renal disease progression in five stages:

1. Early hypertrophy and hyperfunction with increased glomerular filtration and kidney size – at time of diagnosis establishment, 100% of which enter the subsequent stage.

2. Kidney damage without clinical symptoms, with increased glomerular filtration and thickenning of capillary basal membrane after 2-3 years; 30-40% of cases entering the subsequent stage.

3. Starting nephropathy 7-15 years of the disease with normal or slightly decreasing glomerular filtration, advancing glomerulosclerosis, systematic hypertension, and 60-10% progressing to the subsequent stage.

4. Clinically manifest diabetic nephropathy or decreasing glomerular filtration, systematic hypertension, 70-100% entering the subsequent stage.

5. Terminal renal disease, 20-40 years after the diagnosis establishment, glomerular filtration is lower then 10 ml/min.

Patients and methods – Patients: The paper is a part of the study from 1988 carried out at the Pediatric Clinic in Sarajevo. The aim of the study is the evaluation as to what extent and in what number of patients microvascular complications (nephropathy, neuropathy and retinopathy) are present and the establishment of their mutual relationship. Within the research during 1988-90, a transversal section of the presence of nephropaties was done. Renal function was investigated, and the obtained results presented in this paper.

Glomerular kidney function was assessed in 92 children and adoloescents (42 male and 50 female) with insulin dependent diabetes and

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average age of 11.42 years (± 1.28). The children had no laboratory or any other symptoms of renal disease.

Methods – Glomerular filtration rate was established using Chromium Editic Acid (Cr-EDTA) and by taking blood samples every hour, four times.

The values for the control group were, for etic reasons, taken from references (103 ± 13 ml/min/1.73m2) (2).

Statistic processing was done using Mstat-Microsta, Mchart computer software, and the values are shown using mean value (± SD and percentage (%). Significance was tested by Student T test.

Results – Out of 23 diabetic children in the course of the first two years after the diabetes establishent, 65,27% had increased glomerular filtration (2 SD) compared to the referent values. Mean value for the group of patients was 186.18 (± 64.22) ml/min/1.73m2. In the group of children with the disease duration of 3-5 years mean GFR value was 176.52 (I 34.48) ml/min/1.73m2, and 10 out of 24 children had an increased GFR. After 5 years of the disease duration, 39.13% of patients had increased GFR values with mean value of 139.17 (± 31.65) ml/min /1.73m2. In the group of patients with the disease duration of over 10 years, mean GFR value was 146.12 ml/min/1.73m2, and 10 out of 22 children (45, 45%) had divergences from GFR for over 2 sd of referent values (Table 1, Figure 1).

Discussion – It has been established that 65.27% of patients have a significantly increased GFR (Cr-EDTA) in the course of the first two years of the disease.

In Krostroup's study (3) 53% of patients with insulin dependent diabetes had increased GFR values in the same duration of the disease.

Mean GFR value in the group of patients with 3-5 year duration of the disease was 176,52 ± 34,48 ml/min. Bilous (4) finds CR-EDTA clearance increased for 42,7% with respect to normal value. Mean disease duration is 4.68 i.e 12.08 years. In the investigated group of insulin dependent patients, with Hostetter (5) 51% of patients had increased GFR with the mean disease duration of 4.89 years which is very close to the results established in the study (39,13%). Viberti and Haycock (6,7,8) have found an increased Cr-EDTA clearance in 47.3% of patients with diabetes duration of 6.17 i.e 13.44 years. Brochner and Mortensen (9) report increased GFR for 27% with the mean duration of the disease of 7.28 years whereas the relevant percentage is much higher in this study (66,67%). The difference could be explained by the younger age of patients (17.5 ± 3.46) observed in the study compared to Brochner-Mortensen study (44.43 ± 12.03) (9).

Table 1 – Values of GFR (Cr-EDTA) in juvenile diabetics related to duration of disease

Group	control	I	II	III	IV
Duration of disease		0-2	3-5	6-10	>10
No of patients	20	23	24	23	22
Sex (f/m)	18/8	11/12	8/16	10/13	13/9
Age (years)	11.3(3.5)	9.4(3.87)	13.1(3.73)	13.2(3.82)	17.5(3.46)
GFR (Cr-EDTA) (ml/min/1.73m2)	109(13)	186.18(64.22)	176.53(34.48)	139.17(31.65)	146.12(34.95)
% pat.with elevated GFR		65.27% (15/23)	41.67% (10/24)	39.13% (9/23)	45.45% (10/22)

p* NS Control/IV group
p*>.05 Control/I/II/III group.

GFR (Cr-EDTA): glomerular filtration rate with chromium edetics acid.

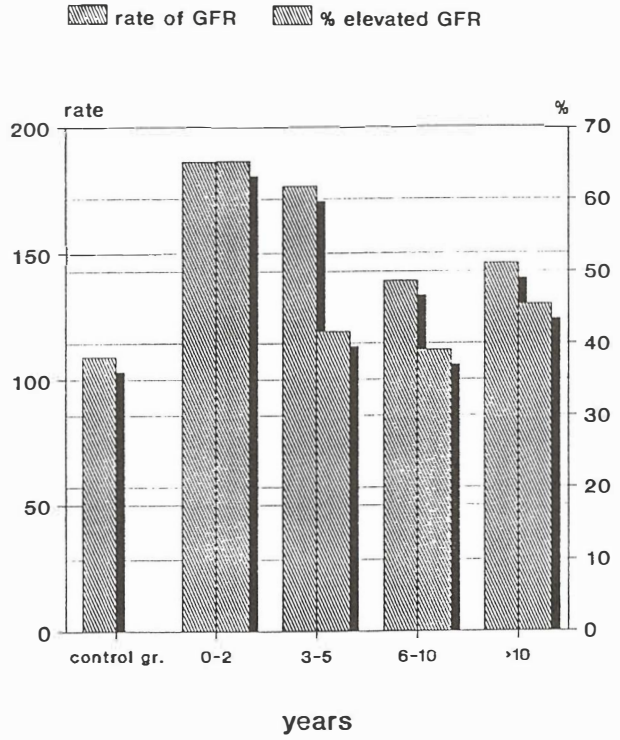

Fig. 1 – Relation rate of GFR and percentage elevated GFR

Conclusion – During the first year of the disease in children and adolescents with insulin – dependent diabetes increased glomerular filtration appears. High values of glomerular filtration are apparent at the time of diagnosis and during the first two years of the disease. With further duration of the disease the glomerular filtration level decreases, which is also described by some other authors (4,10,11,12). Mogensen (1), describing developing stages od diabetic nephropathy, also quotes an increased GFR rate even up to the fifth year of diabetes duration during the stages of hyperfiltration, neprhomegalia and clinically manifest stage, after which the GFR rate gradually decreases.

The markers of affected renal function were of transitory character and mostly disappeared after the stabilisation of the basic disease. On the basis of current knowledge and possibilities of research, future development of diabetic nephropathy cannot be precisely predicted, but we believe their longitudinal observation in diabetic patients necessary.

References

1. Mogensen CE, Christiansen CK, Vitinghus E. The stages in diabetic nephropathy: with emphasis on the stage if incipient diabetic nephropathy. Diabetes 32 (suppl 2): 1983; 64-78.

2. Chantler C, Barrett T. Estimation of glomerular filtration rate from plasma clearence of 51-chromium edatic acid. Arch is Child 1972; 47:613.

3. Kroustroup JP, Gundersen HJG, Osterby R. Glomerular size and structure in diabetes mellitus. Early enlargement of the capillary surface. Diabetologia 1977; 13:207-10.

4. Chavers BM, Bilous RW, Ellis EN, Steffes MW, Mauer SM, Hostetter Th, Troy JC, Brener BM. Glomerular haemodinamics in experimental diabetes mellitus. Kidney Intern 1981; 19:410-15.

5. Hosetetter TH, Troy JC, Brener BM. Glomerular haemodynamics in experimental diabetes mellitus. Kidney Intern 1981; 19:410-15.

6. Viberti GC, Bilous R, Mackintosh D. Monitoring glomerular function in diabetic nephropathy; a prospective study. Am J Med 1983; 74:256-64.

7. Viberty GC, Bending JJ. Early diabetic nephropathy. Adv Nephrol 1988; 17:101-2.

8. Viberty GC, Haycock G, Pickup J, Jarrett R, Keen H. Early functional and morphologic vascular renal consequences of the diabetic state. Diabetologia 1980; 18:173-5.

9. Brochner-Mortensen J, Ditzel J, Mogensen CE, Robro P. Microvascular permeability to albumin and glomerular filtration rate plasma clearence of 51-chromium edetic acid. Arch Dis Child 1972; 47:613.

10. Krolewski AS, Warrm JH, Chistielb AR, Busick EJ, Kahn CR. The changing natural history of nephropathy in type I diabetes. AM J Med 1985; 78:785-94.

11. Selby JV, Fitzsimmons SC, Newman JM, Katz PP, Sepe S, Showstack J. The natural history and epidemiology of diabetic nephropathy. Implications for prevention and control, JAMA 263 1990; (14):1954-60.

12. Steffes MW, Osterby R, Chavers B, Mauer SM. Mesangial expansion as a central mechanism for loss of kidney function in diabetic patients. Diabetes 1989; 38:1077-81.

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PENTAVALENT TECHNETIUM–99m-(V)–DMSA UPTAKE IN AN OCCULT MEDULLARY CARCINOMA OF THE THYROID

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Abstract – This case report describes preoperative 99m-Tc-(V)-DMSA accumulation in a small, nonpalpable, occult medullary carcinoma of the thyroid gland, measuring only 8 x 5 mm.
Complete preoperative, as well as postoperative examination showed no evidence of either intraglandular dissemination, or local or distant metastases. The authors believe that this is the first reported case of positive uptake of 99m-Tc-(V)-DMSA in such a small, occult primary medullary carcinoma of the thyroid.

UDC: 616.441-006.6:615.849.2

Key words: thyroid neoplasms; technetium

Case report

Radiol Iugosl 1991; 25:335-38.

Introduction – Medullary carcinoma of the thyroid (MCT) is a tumor of the parafollicular (C-cells) of the thyroid gland, that secrete calcitonin (CT).

Almost ninety percent of the cases appear sporadically, with the rest occurring in families as a part of multiple endocrine neoplasia (MEN IIa and MEN IIb), with autosomal dominant inheritance, high penetrance and variable expression (1, 2, 3).

The diagnosis of MCT is not difficult in patients with clinical signs of thyroid tumor growth or symptomatic metastases. It is supported by plasma calcitonin assays combined with provocative tests, sonographic examination, fine needle aspiration biopsy (FNAB), and pathohistologic examination.

However, for curative therapy (total thyroidectomy), it is desirable to diagnose the disease early, during nonmetastasized, and if possible, occult tumor stage (1, 2, 3).

Technetium – 99m dimercaptosuccinic acid (DMSA) scintigraphy has been used for the diagnosis of MCT as well as for the localization of metastatic sites and residual tumor (4, 5, 6, 7, 8). Ohta et al. have shown DMSA uptake in a variety of benign and malignant soft tissue and bone tumors (7).

Materials and methods – Technetium-99m-(V)-DMSA was prepared applying a slightly modified procedure, proposed by Jovanović et al. (9).

To a vial of commercially available Tc-99m-(V)-DMSA kit (Boris Kidrič Institute of Nuclear Sciences, Vinča, Yugoslavia) containing 1.0 mg DMSA, 0.12 mg $SnCl_2 \times 2H_2O$, 0.5 mg ascorbic acid and 9 mg NaCl, 1.1 ml of fresh, sterile solution of 0.5% $NaHCO_3$ was added.

Immediately after shaking the vial, 30 mCi of 99mTc pertechnetate in 2.9 ml of physiological saline was added, the total volume being thus adjusted to 4.0 ml. The vial was shaken again and left standing free for 20 minutes at room temperature. A dose of 15 mCi of Tc-99m-(V)-DMSA was administered intravenously to the patient.

The radiochemical purity of the final product (in terms of the fraction of 99m-$Tc0_4^-$) was assessed by paper chromatography on Whatman No. 1, using acetone as a mobile phase (9). The radiopharmaceutical was found to be of appropriate radiochemical purity ($99mTc0_4^- < 1\%$).

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Anterior and posterior images over the whole body were taken 2 hours postinjection of Tc-99m-(V)-DMSA, using a large field-of-view gamma camera, equipped with a low-energy all-purpose parallel collimator.

The calcitonin level in the patient serum was determined by standard radioimmunoassay (RIA-mat Calcitonin II, Mallinckrodt Diagnostics GmbH, Dietzenbach, Germany).

Sonographic examination was performed using a standard real-time machine (Aloka SSD-256) with 5 MHz and 7.5 MHz probes.

Ultrasonically guided fine needle aspiration biopsy was performed using a 22 gauge needle. Fresh, air-dried smears were stained by the Papenheim (May-Gruenwald-Giemsa) method. For MCT cell identification we utilized the Grimelius silver stain (10).

Case report – A 49-year-old woman was under surveillance in our department for five years, because of euthyroid nodular goitre. She had a palpable solitary node, echographically isoechogenic, with small cystic changes, 4 x 1.6 x 2.3 cm large, in the right lobe. Two FNAB's of this nodule showed benign findings.

The patient came for control sonographic examination of the thyroid, when in addition to previously described node, small, hypoechoic, clearly delineated nodule, measuring 8 x 5 mm, in the upper pole of the left lobe of the thyroid was found (Figure 1).

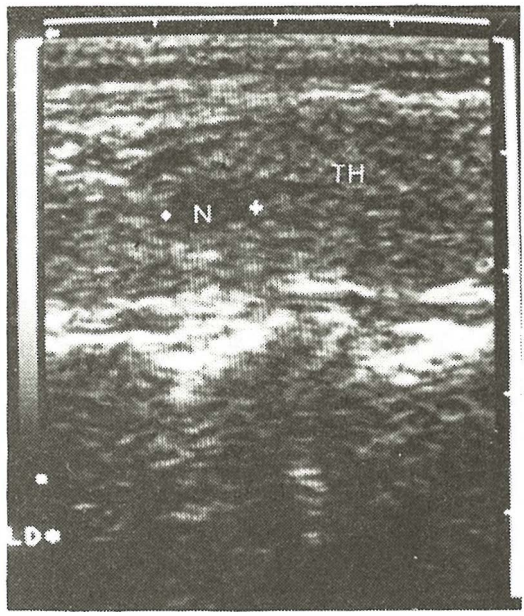
Ultrasonically guided FNAB was performed, and cytologic examination revealed MCT cells. The reaction according to Grimelius was positive and manifested itself by brown-black granules in the cytoplasm of MCT cells (10). Pathohystologic diagnosis confirmed this finding.

The patient was euthyroid with negative thyroid antibodies. Tc-99m pertechnetate and J-131 scans displayed non-homogenous distribution of radiotracers in both lobes of the thyroid.

Biochemical investigations revealed normal basal serum CT levels – 92.2 pg/ml (normal range: 0-150 pg/ml) and 10 minutes after ethanol provocation CT level was elevated in excess of 176.6 pg/ml.

We found normal parathormon, prolactin and ACTH serum levels and normal vanil-mandelic acid urinary level.

Ultrasonography of the upper abdomen was normal, and detailed sonographic examination of neck region was normal, except for changes in the thyroid gland.



+ = cursors on the nodule edges.
N = nodule
TH = thyroid lobe

Fig. 1 – longitudinal ultrasonic scan of the left thyroid lobe (LD), showing hypoechoic, clearly delineated nodule, measuring 8 x 5 mm, in the upper pole. Medullary carcinoma of the thyroid at histopathology.

99m-Tc-(V)-DMSA scintigraphy of the neck, thorax and abdomen was performed and showed accumulation in small area in projection of the upper half of the left thyroid lobe, corresponding to the area in which MCT was situated (Figure 2).

Total thyreoidectomy was performed, and pathohystologic examination in multiple slices confirmed the diagnosis of medullary carcinoma. There was no evidence of tumor cells in thyroid parenchima outside of small nodule.

Postoperative 99m-Tc-(V)-DMSA scintigraphy, as well as neck region sonographic examination failed to reveal any evidence of residual tumor or dissemination.

Postoperative basal and provocation CT levels were normal.

Discussion – There is almost general agreement that in patients with hereditary and sporadic MCT, total thyroidectomy with removal of lymph nodes in the primary lymphatic drainage area of the gland is required (11). To achieve complete removal of tumor it is important to discover disease in early, nonmetastasized, preferably occult stage (1, 2, 3).

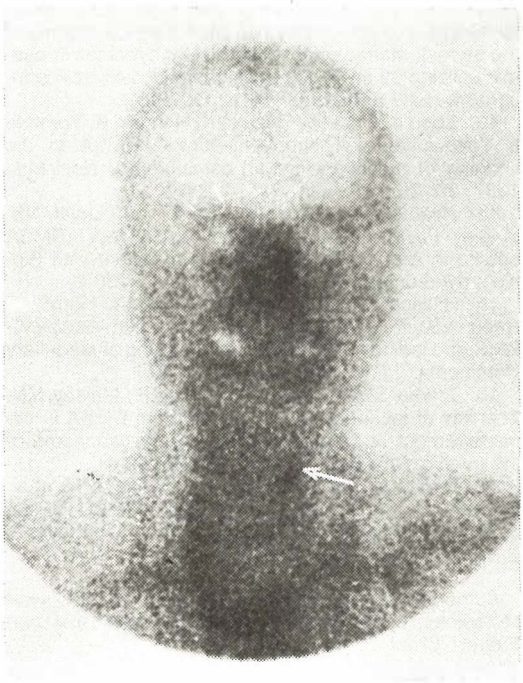


Fig. 2 – 99m–Tc–(V)–DMSA anterior scan of head and neck, with tracer uptake in the upper pole of the left thyroid lobe (arrow), corresponding to area where medullary thyroid cancer is situated.

Role of screening of the patient's relatives by assesment of basal and levels of calcitonin after provocation, sonographic examination and FNAB under ultrasonic guidance is substantial (1, 2).

Up to now, several authors reported more than 50 patients with primary or metastatic MCT who were submitted to 99m-Tc-(V)-DMSA scintigraphy (4, 5, 6, 7, 8, 12, 13, 14, 15). It is considered that convenience and high-image quality make 99m-Tc-(V)-DMSA a valuable adjunct to the currently accepted biochemical method of follow up of MCT patients after thyroidectomy (16).

As far as preoperative accumulation of 99m-Tc-(V)-DMSA in MCT is concerned, Ohta et al., described four MCT patients with hypercalcitoninemia and significant tracer uptake in palpable cervical tumor and metastatic sites (4). Although encouraging, all of these patients had bulk disease that was evident on clinical examination or conventional radiographic studies.

Subsequently, Hilditch et al., reported no uptake in five patients with hypercalcitoninemia (15). These patients were thought to have early disease with only modest calcitonin levels – the subset of patients in whom a sensitive early scintigraphic technique would have the greatest impact.

More recent reports by Ramamoorthy et al. (17), and Clarke et al. (16), have been more favourable. However, all Ramamoorthy's patients appeared to have had known metastases, while Clarke's patients were symptomatic at the time of the study, suggesting advanced disease.

In this report we present a case of occult medullary carcinoma of the thyroid that was diagnosed preoperatively, using ultrasonically guided fine needle aspiration biopsy, cytochemistry analysis, as well as 99m-Tc-(V)-DMSA scintigraphy.

Tumor was limited solely to a small, nonpalpable nodule, measuring only 8x5 mm, with no evidence of either intraglandular dissemination of local or distant metastasis, in course of preoperative, as well as postoperative management.

Since we found positive uptake in such a small tumor preoperatively, we believe that this report could contribute to further evaluation of 99m-Tc-(V)-DMSA scintigraphy as a complementary preoperative diagnostic method in management of medullary carcinoma of the thyroid.

Sažetak

NAKUPLJANJE 99m-Tc(V)-DMSA U OKULTNOM MEDULARNOM KARCINOMU ŠTITNJAČE

Ovaj prikaz slučaja opisuje preoperativno nakupljanje 99m-Tc-(V)-DMSA u malom, nepalpabilnom, okultnom medularnom karcinomu štitnjače, dimenzija 8 x 5 mm.

Temeljite preoperativne, kao i postoperativne pretrage nisu pokazale znakova postojanja intraglandularne diseminacije, kao niti lokalnih ili udaljenih mestastaza. Autori vjeruju da je ovo prvi opisani slučaj pozitivnog nakupljanja 99m-Tc-(V)-DMSA u tako malom okultnom, primarnom, medularnom karcinomu štitnjače.

References

1. Saad MF, Ordonez NG, Rashid KR, et al. Medullary Carcinoma of the Thyroid. A Study of the CLinical Features and Prognostic Factors in 161 Patients. Medicine 1984; 63(6):319-42.

2. Gershengorn MC, Robbins J. Thyroid Neoplasia. In: Green WL ed. The Thyroid. New York: Elsevier, 1987: 325-6.

3. Schwerk WB, Gruen R, Wahl R. Ultrasound Diagnosis of C-cell Carcinoma of the Thyroid. Cancer 1985; 55:624-30.

4. Ohta H, Yamamtoto K, Endo K, et al. A New Imaging Agent for Medullary Carcinoma of the Thyroid. J Nucl Med 1984; 25:223-5.

5. Ohta H, Endo K, Fujita T, et al. Sipple's syndrome with liver tumors examined by iodine – 131 MIBG and technetium – 99m-(V)-DMSA. J Nucl Med 1988; 29:33-8.

6. Clarke SEM, Lazarus CR, Wraight P, Sampson C, Maisey MN. Pentavalent 99mTc-DMSA, 131-J-MIBG, and 99mTc-MDP – an evaluation of three imaging techniques in patients with medullary carcinoma of the thyroid. J Nucl Med 1988; 29:33-8.

7. Ohta H, Endo K, Fujita T, et al. Clinical evaluation of tumour imaging using 99 m Tc-(V) – dimercaptosuccinic acid, a new tumour–seeking agent. Nucl Med Commun 1988; 9:105-6.

8. Patel MC, Patel RB, Ramanathan P, et al. Clinical evaluation of 99 m–Tc (V) dimercaptosuccinic acid (DMSA), for imaging medullary carcinoma of thyroid and its metastasis. Eur J Nucl Med 1988; 13:507-10.

9. Jovanović MS, Zmbova B, Maksin T, et al. Comparative radiochemical and kinetic study of tumorotropic and renal 99m Tc-DMSA. J Radoanal Nucl Chem 1990; 141:91-9.

10. Halbauer M, Črepinko I, Tomić Brzac H, Šimonović I. Fine needle aspiration cytology in the preoperative diagnosis of ultrasonically enlarged parathyroid glands. (In press in Acta Cytologica).

11. Brunt LM, Wells SA Jr. Advances in the diagnosis and treatment of medullary thyroid carcinoma. Surg Clin North Am 1987; 67:263-79.

12. Udelsman R, Mojiminiyi OA, Soper NDW, Buley ID, Shepstone BJ, Dudley NE. Medullary Carcinoma of the thyroid: management of persistent hypercalcitonaemia utilizing 99 m–Tc-(V) dimercaptosuccinic acid scintigraphy. Br J Surg 1989; 76(12):1278-81.

13. Endo K, Ohta H, Torizuka K, Horiuchi K, Yomoda I, Yokoyama A. Technetium–99m(V)–DMSA in the imaging of medullary thyroid carcinoma. J Nucl Med 1987; 28: 252-3.

14. Adams BK, Fataar A, Byrne MJ, Levitt NS, Magley PJ. Pentavalent technetium–99M–(V)–DMSA uptake in a pheochromocytoma in a patient with Sipple's syndrome. J Nucl Med 1990; 31(1):106-8.

15. Hilditch TE, Connell JMC, Elliott AT, Hurray T, Reed NS. Poor Results with Technetium–99M–(V)-DMS and iodine–131 MIBG in the Imaging of Medullary Carcinoma. J Nucl Med 1986; 27-1150-3.

16. Clarke SEM, Lazarus C, Mistry R, Maisey MN. The role of technetium–99m pentavalent DMSA in the management of patients with medullary carcinoma of the thyroid. Br J Radiol 1987; 60:1089-92.

17. Ramamoorthy N, Shetye SV, Pandey PM, et al. Preparation and evaluation of 99m TC–(V)–DMSA complex: studies in medullary carcinoma of thyroid. Eur J Nuci Med 1987; 12:623-8.

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RADIOTHERAPY OF INTRACRANIAL CHILDHOOD TUMOURS WITH 9 MV LINEAR ACCELERATOR (NEPTUN 10–P)

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Abstract – The authors have investigated the possible ways of radiotherapy in childhood for malignant CNS tumours, emphasizing the significance of postoperative radiotherapy. The presentation of their practical work is based on their own patient groups. Between 1986 and 1990 altogether 30 patients, under the age of 15 years, were treated for CNS primary malignancies. The crude survival rate of the patients was 24.5 months.

UDC: 616.831-006.6:615.849.12

Key words: brain neoplasms; radiotherapy

Orig sci paper

Radiol Iugosl 1991; 25:339-44.

Introduction – The tumours of the central nervous system are the most frequent solid tumours of childhood. However, this statement is true only in general – analyses based on age, sex and histology give different results. The frequency of these tumours among childhood malignancies is 20–25 percent (1, 2, 3). According to British and US registrations, out of one million children under the age of fifteen years approximately 100 develop new malignant tumours per year, with 20-25 tumours of the central nervous system (4). A majority of the cases occur in the second part of the first decade of life.

Considering the frequency of these tumours, radiotherapists are constantly challenged by the task of applying the appropriate irradiation treatment. The aim of the paper is to provide a survey of the medical activity at the Chair of Radiotherapy, Postgraduate Medical University. We examine the mode of postoperative radiotherapy of solid tumours, moreover, the radiotherapy of recurrences and inoperable tumours excluding the manifestations of systemic diseases in the central nervous system, metastatic brain tumours, and spinal cord tumours.

Material and methods – The Neptun 10p linear accelerator has been used in the National Institute of Oncology (Chair of Radiotherapy, Postgraduate Medical University) since October 1985. This equipment was used for the treatment of children for the first time in 1986 (Figure 1). The accelerator produces a 9 MV X-ray and 6, 8 and 10 MeV energy electron beams. By means of a continuously adjustable diaphragm–system optional size fields can be applied ranging from 3x3 cm to 40x40 cm by X-rays, and from 3x3 cm to 25x25 cm by electron beam. The 9 MV energy X-ray beam is suitable for the treatment of intracranial childhood tumours.

Altogether 30 children suffering from intracranial primary malignant tumours were treated with the Neptun 10p linear accelerator between 1986 and December 31, 1990. The youngest patient was nine months old and the oldest 14 years, the mean age was 8.1 years. Twenty–one of them were males and nine females – ratio 2.3:1. Table 1 shows the localization and histology of the tumours.

Treatment planning was performed in all children. The real anatomic situation was reproduced by the help of a CT scan. The target volume

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can be determined by the CT scan and by knowledge of all clinical data, i.e. localization, extent, previous status in case of an earlier operation, preoperative CT picture, surgical data as well as histology. The area to be protected has to be defined for optimal beam direction, number and size of the fields.

The application of two or more fields, with different beam directions for the target area usually provides optimal dose distribution (Figure 2a–b). By irregular geometry of the tumour the optimal dose distribution can be assured by wedged fields. Rotation of the irradiating head between 0 and 365 degrees in both directions can be carried out by Neptun 10p. This has two practical advantages: the first one is that the patient can be treated in a horizontal position, on his back and in this way the precision and reproductivity of the irradiation can be assured.

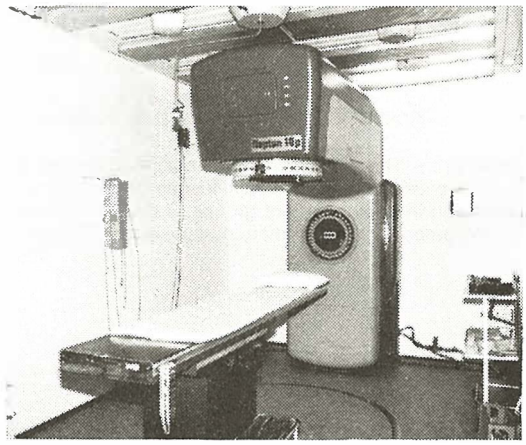


Fig. 1 – The Neptun 10p linear accelerator of the National Institute of Oncology

Table 1 – Histology and localization

	PNET	medullobl.	astrocyt.	glioma	ependym.	small cell. tu	No data
Post. scala		13	1		1		2
Cerebrum	1		3	1	1	1	2
Chiasma/n. opt.			1				2
Cranio–spinalis			1				
Total	1	13	6	1	2	1	6

Furtheremore, the danger of the patient movement during irradiation is the smallest in this horizontal position. The second advantage is the possibility of isocenter technology application, i.e. the geometrical center of the volume to be irradiated is the axis of rotation, and by the rotation of the irradiating head around this axis we can adjust the desired directions of the beam (Figure 3a–b)-

Out of the children treated in our Institute, radiotherapy was applied in 19 postoperative, 9 inoperable and 3 relapsing cases. One patient received preoperative radiotherapy. Thirty–two series of treatment were given to 30 patients. In one patient the reason for this was a recurrence that developed four months after radiotherapy, so complementary irradiation had to be applied – thus, this patient has been included in both the postoperative and the recurrent tumour groups (Gy. L. age: six years, ependymoma papillare). In the case of another patient repeated manifestation developed over the area of the medulla oblongata after 30 Gy of postoperative irradiation. Thus, the therapy was continued as the radiotherapy for an inoperable tumour.

We did not apply any chemotherapy in our Institute.

The doses delivered in postoperative and inoperable cases ranged from 44 to 60 Gy – average, 52 Gy (Fig. 4a, b, c). The maximal dose of preoperative radiotherapy was set at 30 Gy. It is impossible to determine the exact dose for recurring tumours because of some other influencing factors, the most important being the previously irradiated volume and the total dose. The daily fractions were 1.5 or 1.8 Gy.

The distribution of tumours according to age is shown in Table 2.

Results – Our results can be summarized as followas: The average rough survival rate was 24.5 months, with the average of those living 25. 3 months (16 patients), and the average of those deceased 23.3 months (10 patients). Altogether

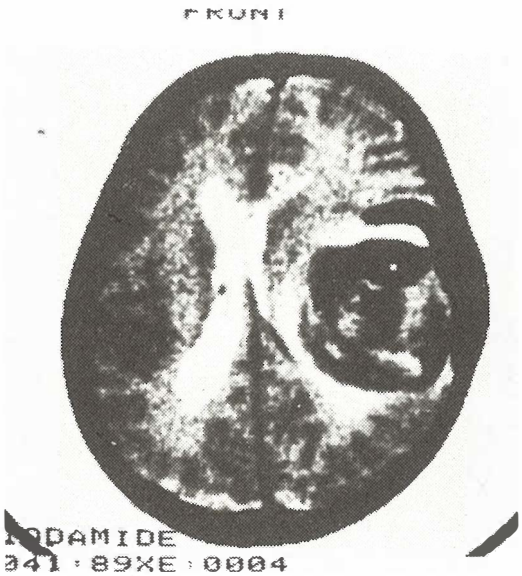


Fig. 2a – CT–topometry. D.F., male, six years old. Dg: glioma cerebri•

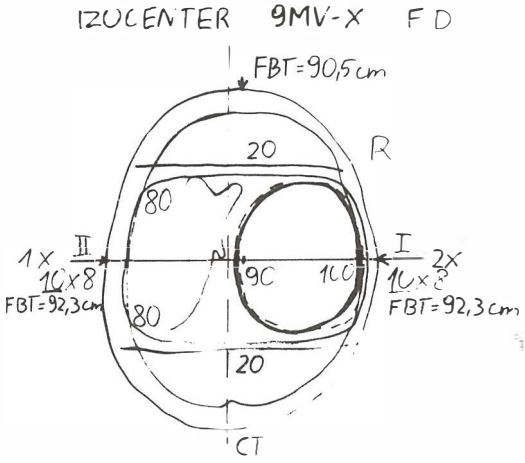


Fig. 2b – Irradiation plan, two opposing fields, weight factor 2:1, linear accelerator 9 MV. Field size 10x8 cm.

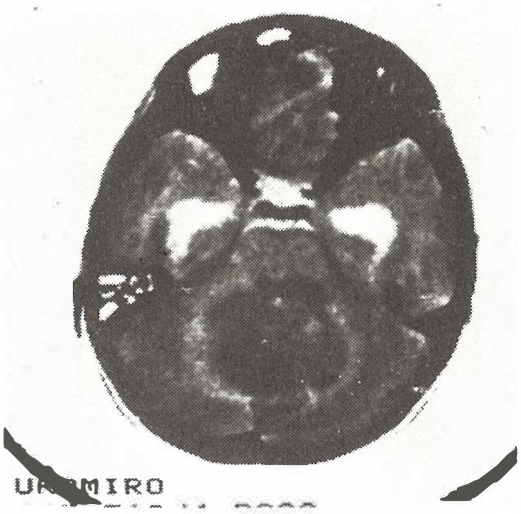


Fig. 3a – A.K. 7–year old child. Preoperative CT scan of the child who was operated on for medulloblastoma. The treatment plan was made on the basis of a preoperative CT scan.

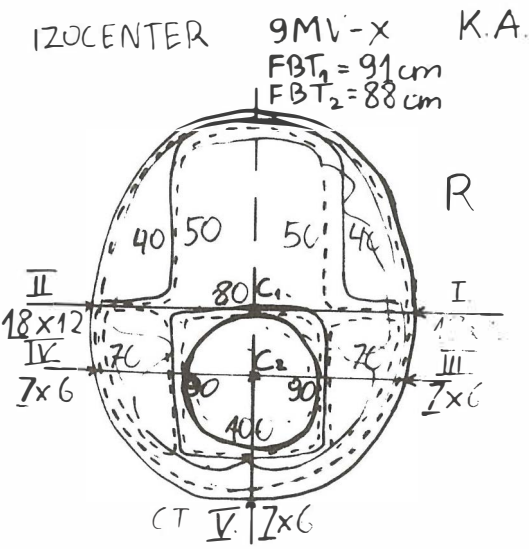


Fig. 3b – CT-based treatment planning. Irradiation to five fields with isocenter technology. Three 7x6 cm and two 18x18 cm fields.

we were able to follow 26 patients, 4 patients were lost to follow–up.

A longer survival rate – 31.8 months – in the case of medulloblastomas implies a favourable prognosis as the average survival rate of the deceased is only 27.8 months. However, this difference is not a significant point (5). This statement is also true of the group without histological diagnosis, both with regard to expected survival as well as to its statistical significance. We were unable to evaluate other histological groups because of the low number of patients.

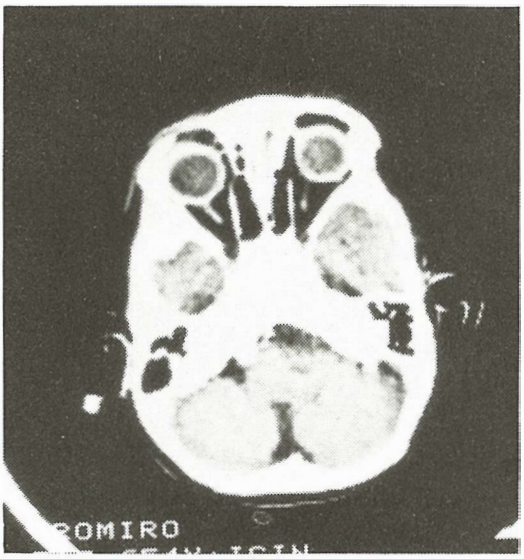


Fig. 4a – Inoperable tumour of the posterior scala, unknown histology. CT-based treatment planning M.B. 3-year old boy

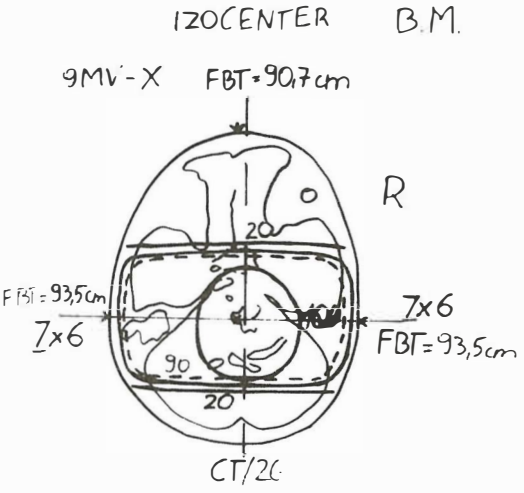


Fig. 4b – Irradiation treatment plan

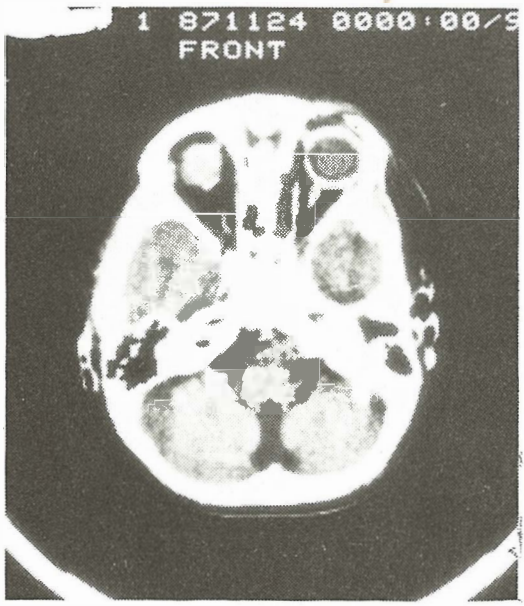


Fig. 4c – Regression is observable on the follow–up CT scan, six weeks after completed irradiation

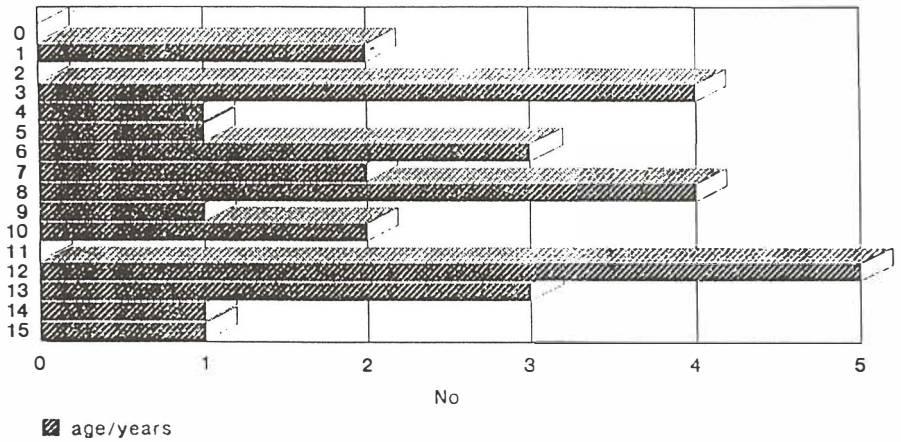
Discussion – Radiotherapy of the primary CNS tumours in childhood can be indicated as follows:

1. Postoperative radiotherapy – the most common form. Following radical extirpation of the tumour, the application of radiotherapy significantly increases the chances of survival. According to the data of Mork and Locken (6) the five-year survival of children with ependymoma who were treated by operation alone was 24 percent, while the application of postoperative radiotherapy increased this rate to 60 percent. Sheline and his associates (7) found the 5–, 10–, and 20–year survival trates to be 18, 10 and 0 percent, respectively in patients treated by operation alone. However, this rate could be increased to 46, 25 and 23 percent, respectively with postoperative radiotherapy. These data prove the effectiveness of postoperative radiotherapy, especially in radiosensitive neoplasms.

2. Radiotherapy of inoperable intracranial tumours – Regarding operability, the primary factors are the size and/or localization of tumour although other clinical aspects – performance status, age, etc. – should also be considered. In favourable cases, originally inoperable tumours were rendered operable by the application of an appropriate total dose, this form of treatment becoming recognized **preoperative radiotherapy.**

3. Radiotherapy of recurrent tumours is indicated according to the localization, size and histology of tumour, and the previous radiation dose. This form of treatment is applied generally with palliative intent both in the case of single or multifocal recurrences.

Table 2 – Age distribution



Whatever the indication may be, the irradiation of primary childhood tumours of the central nervous system must be carried out by supervoltage radiation: X-ray and electron radiation of circular or linear accelerators, particularly by cobalt – or caesium teletherapy. According to the young age of the patients the selection of an appropriate radiation source and a proper treatment planning are necessary, with special emphasis on some unique aspects:

a. The area to be irradiated is located in a bone–surrounded cavity. In that case radiation has to penetrate through a number of different–density substances. As it is well known from radiation physics, critical zones develop on the borders of the substances with different density – first of all as a result of secondary electron rays. Another point of consideration is that the absorption of the ionizing radiation depends on the Ca content of the bones. The younger the patient, the smaller the rate of calcium in the bones. Thus, the absorbed radiation dose is also smaller than by adults. Further differences can be observed in certain age groups.

b. The cellular radiosensitivity of growing children's tissues – including the nerve cells – differs from the radiosensitivity of the mature cells of adults. This has to be taken into consideration with regard to the degree of the acute radiation reaction during and after treatment, and later on in the development of late side effect evaluation.

c. As a result of the unique circumstances, radiotherapy necessitates higher technological and personnel conditions. More advantageous applications are, for instance, the multiple direction radiation treatments, the use of wedged fields, and isocenter technology.

d. The improving results and increasing number of cured children raise the question of late, frequently permanent radiation effects. Their incidence must be followed for prophylaxis and rehabilitation. Both radiation therapy and cytostatic treatment can cause the development of damage such as somatic mutations, genetic disorders, disturbances of the endocrine system, growth disturbances, and the decrease in the intelligence quotient (8, 9).

Conclusion – We have investigated the possible ways of radiotherapy in childhood for malignant CNS tumours, emphasizing the significance of postoperative radiotherapy. Between 1986 and 1990 we treated altogether 30 patients under the age of 15 years, for CNS primary malignancies. The crude survival rate of our patients was 24.5 months.

References

1. Farwell IR, Dohrmann GH, Flannery JT. Cancer 1977;40:3123.
2. Gyenes G. Magyar Onkológia 1981; 25:235.
3. Gyenes G, Németh Gy. Sugártherápia – Medicina. Budapest, 1986.
4. Gyenes G. Magyar Onkológia 1977;21:231.
5. Juvancz I, Paksy A. Orvosi biometria, Medicina BP, 1982.
6. Mørk SJ, Løcken AC. Cancer 1977;50:907.
7. Scheline GE. Cancer 1977;39:873.

8. Sasaki U, Haru M, Watanabe S. JP H Clin Oncol 1988;18:84.
9. Schuler D. Orvostudomány 1982;33:445.
10. Fritz P, Becker F, Kuttig H, Winkel K. Strahlenther, Onkologie 1989;165:571.
11. Goldwein JW, Glauser TA, Packer RJ et al. Cancer 1990;66:557.
12. Gyenes G. Radiobiol Radiother 1980;21:208.
13. Jones, P.M. The Practitioner 1979;222:221.
14. Kocsis B, Pap L, Somló P, Gyenes G, Kontra G. Magyar Onkológia 1989;33:173.
15. Lanering B, Marky J, Nordborg C. Cancer 1990;66:604.
16. Lindgren M. Strahlentherapie 1974;147:109.
17. Scherer E. Strahlentherapie, Springer Verlag, 1989.
18. Suc E, Pons A, Roche H et al. Acta Neurochir 1989;97:19.
19. Veath JM. Childhood Cancer Triumph over Tragedy. Basel, München, Paris, London, New York: S. Karger 1982.

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THE EFFECT OF NEW UNDERSTANDING OF CURABLE BREAST CANCER AND RELATED WITH THAT CHANGED TREATMENT APPROACH ON FIVE–YEAR DISEASE–FREE SURVIVAL AND OVERALL SURVIVAL OF BREAST CANCER PATIENTS

Lindtner J, Eržen D

Abstract – A comparison of 5–year disease–free survival and overall survival in two groups of breast cancer patients treated at the Institute of Oncology in Ljubljana in the years 1976-1977 (287 pts) by surgery and irradiation, and in the years 1982–1985 (318 pts) by surgery, chemotherapy and irradiation, has pointed out a favourable effect of adjuvant systemic treatment on the survival of patients with unfavourable prognostic factors.

UDC: 616.19-006.6:615.849.5

Key words: breast neoplasms; survival analysis

Orig sci paper

Radiol Iugosl 1991; 25:345-9.

Introduction – Breast cancer st. I and II is generally believed to be a surgically curable disease if diagnosed on time and treated by an adequate intervention. This is almost a century old belief which can hardly be shattered by more recent knowledge on curable cancer as a systemic disease which, however, fails to be detected by the existing diagnostic methods (1). As a result of these discoveries, in the last two decades new treatment approaches have been introduced in oncology, in the first place additional systemic treatment, i.e. the so–called adjuvant cytostatic and hormonal therapy.

At the Institute of Oncology, the results of such changed attitude became apparent in the decade between 1976-1985: thus, by 1975, adjuvant systemic treatment would have been regareded as a hardly acceptable novelty whereas in 1985 it was *vitium artis* if at least certain patients with operable breast cancer were not treated by adjuvant chemotherapy. Is it therefore exaggerated to call that decade, at least with reference to the treatment in breast cancer st. I and II, »a decade of changes«?

The aim of the present study is to point out how the mentioned changed understanding of curable breast cancer and accordingly changed approach to its treatment reflects on the 5-year disease–free survival and overall 5–year survival of these patients.

Material – The research was based on historic data of 605 patients with breast cancer stage I and II, treated at the Institute of Oncology in Ljubljana from January 1, 1976 to December 31, 1985. Patients over 70 years of age, as well as pregnant, breast–feeding and those in whom breast cancer treated during the appointed time period was not a primary malignancy, were excluded.

The selected patients were distributed into two groups that could be compared to each other in order to provide an answer to the question defined in the aim of this study:

Group A comprised 287 patients treated in the years 1976 and 1977, whereas Group B consisted of 318 patients treated during the period 1982-1985.

The comparability of both groups by specified prognostic factors is given in Tables 1 and 2.

Differences in treatment approach are evident from Table 3.

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Table 1 – Comparability of the observed groups of patients

Observed parameter	Group A ($N_a = 287$)	Group B ($N_b = 318$)
1) Mean age	51 yrs	49 yrs
2) Menopause	45%	38%
3) Primary tumor size		
up to 20 mm	40%	47%
over 50 mm	0%	3%
4) Rate of poorly differentiated primary tumors (grade III)	33%	38.7%
5) Rate of patients with negative lymph nodes	50.5%	43%

Table 2 – Comparability of patients with histologically positive lymph nodes

Observed parameter	Group A ($N_{a1} = 142$)	Group B ($N_{b1} = 181$)
1) Number of positive lymph nodes 1-3	59.8%	54.6%
10 or more	12.6%	20.9%
2) Invasion through lymph node capsule	45.7%	58.6%

Table 3 – Treatment methods in A and B groups of patients

Treatment	Group A	Group B
1) Mastectomy	100%	82.7%
2) Breast resection	0	17.3%
3) Postoperative irradiation	30.6%	4.4%
4) Adjuvant chemotherapy	0	40.2%
5) Perioperative chemotherapy	0	54.4%

Results – Five-year disease-free survival and overall survival of patients in the observed groups is graphically presented in Figure 1.

Five–year disease–free survival and overall survival of patients with negative axillary lymph nodes is presented in Figure 2.

Five–years disease–free survival of patients distributed according to prognostic categories is given in Table 4.

Discussion – Here it should be pointed out again that this study was not aimed to evaluate the effect of one or the other treatment modality on disease–free survival or overall survival, but rather to present how the changed approach to the treatment of patients with curable breast cancer reflected on the course of disease during the first five years since the beginning of therapy. This is most evident from Table 3 and the respective totals of percentages in the 1st and

Table 4 – 5-year cure of observed patients distributed into prognostic classes

Class	1976 – 1977 No. of patients	1976 – 1977 % of cure	1982 – 1985 No. of patients	1982 – 1985 % of cure
1) $N_0 G_1$	47	87	44	89
2) $N_0 G_2$	70	84	38	87
3) $N_0 G_3$	28	75	55	67
4) $N_1 G_{1,2} P_0$	48	65	53	72
5) $N_1 G_{1,2} P_1$	26	58	58	66
6) $N_1 G_3 P_0$	29	41	21	58
7) $N_1 G_3 P_1$	39	29	49	45

Legend: N – lymph nodes
G – grade of malignancy
P – l.n. capsule invasion

Table 5 – 5-year survival of observed patients distributed into prognostic classes

Class	1976 – 1977 No. of patients	1976 – 1977 % of survival	1982 – 1985 No. of patients	1982 – 1985 % of survival
1) $N_0 G_1$	47	98	44	95
2) $N_0 G_2$	70	84	38	87
3) $N_0 G_3$	28	82	55	78
4) $N_1 G_{1,2} P_0$	48	79	53	81
5) $N_1 G_{1,2} P_0$	26	77	58	66
6) $N_1 G_3 P_0$	29	48	21	76
7) $N_1 G_3 P_1$	39	44	49	57

Legend: N – lymph nodes
G – grade of malignancy
P – l.n. capsule invasion

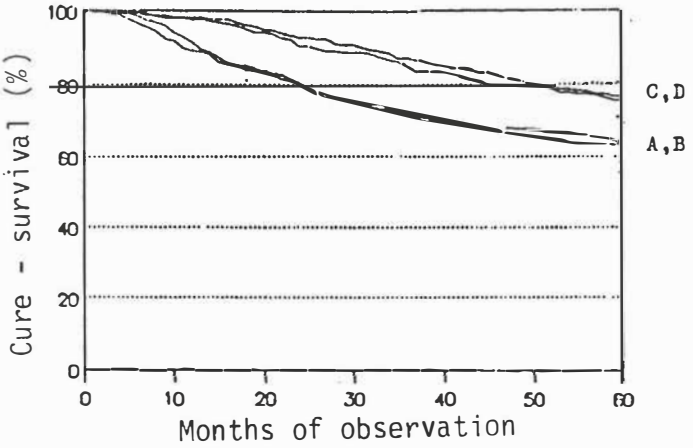
2nd columns: thus the former presents what happened with the patients, whereas the latter specifies the method of treatment which was obviously different. The present work actually conveys just this message and nothing more.

The decision to define the period between 1976-1985 as »the decade of changes« has been made for technical reasons:

In that period, diagnostic workup and consequential follow up of patients with curable breast cancer treated at the Institute of Oncology in Ljubljana was improved in accordance with the recommendations of SASIB research group (Scando–Afro–Swiss International Breast Cancer Study, Lausanne, Switzerland) which was joined also by our Institute. The comparison presented in Tables 1 and 2 is not possible for older patients. Also, the apparently small number of patients included in group B during the years 1982–1985 requres an explanation: though the number of patients with curable breast cancer treated yearly at the Institute of Oncology did not significantly change, the patients from other Yugoslav republics had to be excluded from the

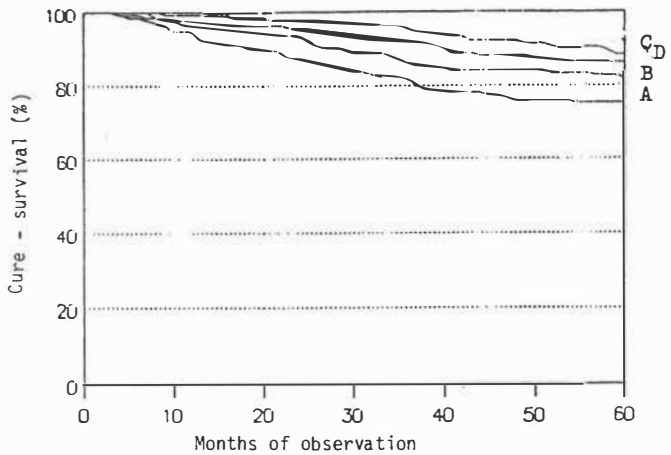
study as their regular follow up was practically not possible.

As to the comparability of our groups of patients under investigation, the only statistically significant difference was found between the patients with positive and those with negative axillary lymph nodes. Though we cannot explain this difference, it does not seem to be of relevance for the message conveyed by our report, as each group was represented independently. With regard to the tumour volume, it should be pointed out that in group A, the criteria for tumour



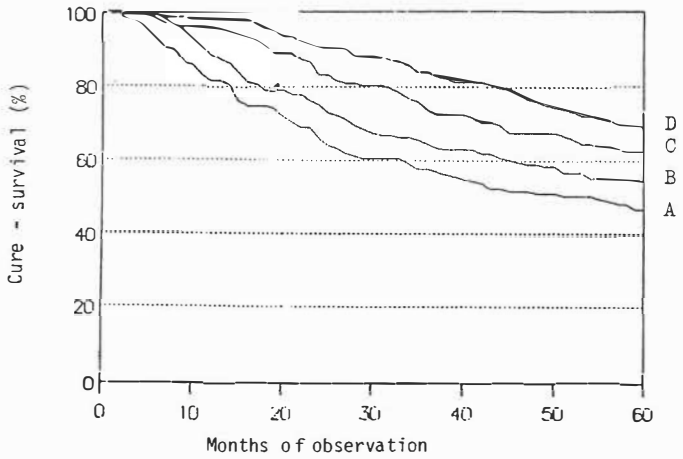
Legend:
A – cure rate in 287 patients treated in the years 1976–77
B – cure rate in 318 patients treated in the years 1982–85
C – survival of 287 patients treated in the years 1976–77
D – survival of 318 patients treated in the years 1982–85

Fig. 1 – Five-year disease-free survival and overall survival in 605 patients with breast cancer St I and II, treated in the years 1976–1985 at the Institute of Oncology in Ljubljana



Legend:
A – cure rate in 142 patients treated in the years 1976–77
B – cure rate in 182 patients treated in the years 1982–85
C – survival of 142 patients treated in the years 1976–77
D – survival of 182 patients treated in the years 1982–85

Fig. 2 – Five-year disease-free survival and overall survival in 282 patients with breast cancer St I and II and negative axillary lymph nodes, treated in the years 1976–1985 at the Institute of Oncology in Ljubljana.



Legend:

A – cure rate in 145 patients treated in the years 1976–77

B – cure rate in 137 patients treated in the years 1982–85

C – survival of 145 patients treated in the years 1976–77

D – survival of 137 patients treated in the years 1982–85

Fig. 3 – Five-year disease-free survival and overall survival in 323 patients with breast cancer St I and II and positive axillary lymph nodes, treated in the years 1976–1985 at the Institute of Oncology in Ljubljana.

operability determination were strictly defined by T–symbol, whereas in group B also breast cancer classified as T3a were considered curable.

Though in our discussion we try to avoid drawing conclusions on the relevance of particular treatment approaches, Table 3 still calls for some further explanation: Evidently, the patients in group A did not receive any primary systemic therapy; these were the patients with negative axillary lymph nodes and tumours in the anterior median third of the breast, who received postoperative irradiation. This treatment, however, was not applied invariably, but depended rather on the decision of individual physicians. Even greater diversity of opinions was seen with reference to the need of postoperative irradiation in patients with positive lymph nodes. Therefore, our Institute decided to join the aformentioned international prospective randomized study according to which every other patient with positive lymph nodes was subjected to postoperative irradiation.

Likewise, every other patient with negative lymph nodes from group B underwent additional systemic therapy: thus 69 of 137 received a perioperative dose of CMF chemotherapy according to our prospective randomised clinical study (LBCS V) (2). As a rule, group B patients with positive lymph nodes were invariably subjected to either hormonal or cytostatic chemotherapy. As to the latter treatment modality, in some patients cytotoxic drugs were applied perioperatively, whereas others received classical postoperative chemotherapy or a combination of both regimens.

Figures presenting the data on disease-free and overall survival do not require any further comment. The noticeable differences are without statistical significance. In an attempt to present possible differences, all the patients were further distributed into different prognostic subgroups. Thus, the patients with negative lymph nodes are divided into three classes according to malignancy grade of the primary tumour (in this distribution, also the tumours which are generally not classified according to their malignancy grade were included in grade III subgroup). The patients with positive lymph nodes were distributed into 4 prognostic classes according to the criteria considered in the randomization by SASIB group. Some positive differences have been observed in prognostically unfavourable subgroups, though the differences were not statistically significant owing to a small number of cases. Our study supports the well known (3) and subsequently confirmed opinion on the value of adjuvant systemic treatment in patients with early breast cancer.

It further points out that an objective assessment of the significance of individual treatment approaches requires a substantially larger num-

ber of patients than can be collected within a reasonable period of time by a single oncological center, and therefore, multicentric collaboration between different oncological institutions in this field is of essential importance.

References

1. Fisher B, Redmond C, Fisher ER, NSABP investigators. The contribution of recent NSABP clinical trials of primary breast cancer therapy to an undertanding of tumour biology – an overview of findings. Cancer 1980; 46:1009-25.

2. Ludwig Breast Cancer Study Group: Randomized perioperative in operable breast cancer: The Ludwig trial V. Recent Results Cancer Res 1989; 115:43-53.

3. UK–BCTSC/UICC/WHO (1984) Review of mortality results in randomized trials in early breast cancer. Lancet II: 1205.

4. Adjuvant Systemic Treatment for Breast Cancer Metaanalysed, LANCET 1989;1:30-84.

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FACULTY OF ELECTRICAL AND COMPUTER ENGINEERING[1], UNIVERSITY OF LJUBLJANA, INSTITUTE OF ONCOLOGY[2], LJUBLJANA

LOCAL TREATMENT OF FIBROSARCOMA SA-1 AND MALIGNANT MELANOMA B-16 SOLID TUMORS IN MICE BY ELECTRICAL DIRECT CURRENT: A PRELIMINARY REPORT

Miklavčič D[1], Serša G[2], Vodovnik L [1], Novaković S[2], Bobanović F[1], Reberšek S[1]

Abstract – Low level direct current (1.0 to 1.8 mA) was employed as an antitumor agent in two different murine tumor models, fibrosarcoma Sa-1 in A/J mice and malignant melanoma B-16 in C57 Bl/6 mice. Single shot treatment with direct current (1.0, 1.4 and 1.8 mA) of one hour duration was performed after tumors reached initial tumor volume (V_0) 48.2±7.9 (n=53) and 45.2±7.5 (64) in Sa-1 and B-16 model respectively (AM±STD). Direct current was deliverad via multiple needle electrode array (Pt-Ir alloy, 90-10%), where three electrodes (cathodes) were inserted directly into the tumor and two electrodes (anodes) were placed subcutaneously in tumor vicinity. Escalating doses of electrotherapy resulted in both tumor models with proportional increase in achieved growth delay which was 4.1±0.8 (n=19) days at 1.0 mA and 11.8±0.9 (n=10) days at 1.8 mA in fibrosarcoma SA-1 and 8.6±0.6 (n=23) days at 1.0 mA and 16.8±0.8 (n=6) in melanoma B-16. In the later tumor model also 4%, 10% and 40% cures were achieved by electrotherapy with 1.0, 1.4 and 1.8 mA of one hour duration respectively. After ET in both tumor models temporal tumor remission was obtained at higher current levels but in most cases tumor regrowth occurred. From the results obtained it is evident that ET as described is a potential regional cancer treatment modality.

UDC: 616-006.327.04:615.84

Key words: fibrosarcoma; melanoma; electromagnetic fields-therapeutic use

Prelim report

Radiol Iugosl 1991; 25:351-3.

Introduction – Although cancer is a very old disease known already in ancient cultures, there is still need to search new cancer treatment modalities since many clinical cases do not respond to established approaches. There has been few reports describing low level direct current (DC) as a possible antitumor agent on different murine tumor models (1-3) and in clinic (4). The objective of our study was to investigate the effect of electrotherapy (ET) on two new murine tumor models. The protocol was based on our previous research where the effects of DC polarity, current level, ET duration and the number of electrodes were studied (5,6).

Materials and methods – Inbred A/J and C57 Bl/6 animals of both sex were purchased from the Institute Rudjer Bošković, Zagreb, Croatia and were eight to twelve weeks old at the start of experiment. Animals were kept in groups of five to eight in plastic cages at natural day/light cycle, constant room temperture 24°C and were fed ad libitum. Subcutaneous solid tumors fibrosarcoma (Sa-1) syngeneic to A/J and malignant melanoma (B-16) syngeneic to C57 Bl/6 were initiated by subcutaneous injection of 5.10^5 and 7.10^5 tumor cells dorsolaterally respectively. Single cell suspension was obtained from ascitic fluid of tumor bearing animals for Sa-1 and by gentle mechanical disaggregation from viable tumor parts for B-16. Cell viability was determined by trypan blue exclusion test and was more than 90%. After the tumors reached initial tumor volume (V_0), 48.2±7.5 (n=53) in Sa-1 and 45.2±7.5 (64) B-16 tumor model, they were subjected to single-shot electrotherapy. DC was delivered through Pt-Ir needle electrodes (∅=0.7 mm) inserted (three electrodes, 18 mm long, insulated except 3 mm tip) directly into tumor and (two electrodes, 20 mm long) subcutaneously in tumor vicinity (5 mm medially and laterally from tumor edge). Electrodes inserted into tumor were connected with single lead to negative terminal and those inserted subcutaneously in tumor vicinity to positive terminal of constant current source designed and manufactured at Faculty of Electrical and Computer Engineering, Ljubljana, Slovenia. Total DC of 1.0 mA, 1.4 mA, and 1.8 mA was passed through tissue for one hour. Control group was treated in the same way except for the current flow. During ET, animals were firmly fixed and they showed no obvious discomfort, therefore no anasthesia was used. Therapy effect was asses-

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sed by measuring three mutually orthogonal tumor diameters (e_1, e_2, e_3) on each day following ET, and the tumor volume was calculated (eq.1). From tumor growth curves the time needed to double initial tumor volume (TD) was determined for each tumor individualy, and growth delay (GD) was calculated (eq. 2)

$$V = \frac{\pi \cdot e_1 \cdot e_2 \cdot e_3}{6} \quad 1$$

$$GD_x = \frac{1}{n}\sum_{j} TD_{xj} - \frac{1}{m}\sum_{i} TD_{ci} \quad 2$$

where c is index of control and x of specific ET group, i and j are indexes of animals within both groups running from 1 to m and 1 to n in control and ET group respectively. Corresponding standard deviation σ was calculated (eq. 3) with ν degrees of freedom (eq. 4)

$$\sigma^2 = \frac{(n-1)\cdot\sigma_x^2 + (m-1)\,\sigma_c^2}{n+m-2}\left(\frac{1}{m}+\frac{1}{n}\right) \quad 3$$

$$\nu = n + m - 2 \quad 4$$

where σ_x and σ_c are experimental standard deviations in experimental and control groups.

Results were statistically evaluated employing non-parametric Mann-Whitney Rank-Sum test on each day following ET, comparing the medians of tumor volumes in control and specific ET group.

Results and discussion – Time from inoculation to performance of ET was 7 and 10 days in Sa-1 and B-16 respectively. Tumor volume doubling time (TD) in control groups was 1.8±0.6 days (n=15) in Sa-1 and 2.5±0.7 days (20) in B-16 tumor model. At 'doses' 1.4 mA and 1.8 mA temporal tumor remission was obtained. In most of the cases tumor regrowth occurred within few days. Tumor growth curves are presented in Figure for Sa-1 (left) and for B-16 model (right). Tumor growth delay was statistically highly significant on each day following the ET ($p<0.0001$ for six days after ET). Animals, in which no tumor regrowth occurred within 30 days after ET, were pronounced as tumor free (S) and accordingly, the percentage of cures (C) was calculated (eq. 5).

$$C = \frac{\text{number of tumor free animals}}{\text{number of all animals in specific ET group}} \cdot 100\% \quad 5$$

Different susceptibility of Sa-1 and B-16 was evident from GD and C and it remains to be explained whether it is a result of different structure of Sa-1 and B-16 tumors, or is it due to the differences between tumor cell strains. At least partially the difference in tumor response to ET between both models employed may be explained by the difference in initial tumor volumes between Sa-1 and B-16 models ($p<0.01$: single tailed Student t-test).

From the results obtained in our study it is evident (Table, Figure) that ET as performed, although still in its infancy, is an effective potential regional cancer treatment modality comparable to other established approaches. We have observed no side effects such as tissue burns nor any obvious discomfort in animals during ET.

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References

1. Humphrey C E and Seal EH. Biophysical approach toward tumor regression in mice. Science 1959; 130: 388-90.

2. David SL, Absolom DR, Smith CR. Effect of low level direct current on *in vivo* tumor growth in hamsters. Cancer Res 1985; 45: 5625-31.

3. Marino AA, Morris D and Arnold T. Electrical treatment of Lewis lung carcinoma in mice. J Surg Res 1986; 41: 198-201.

Table 1 – Single-shot electrotherapy effect on tumor growth by growth delay (GD), number of tumor free animals (S) and percentage of cures (C) for each specific ET group together with number of animals (n) included in groups.

	Sa-1			B-16		
	GD (days)	n	C	GD (days)	n	C
ET 1.0 mA	4.1±0.8	19	0%	8.6±0.6	23+1S	4%
ET 1.4 mA	7.2±0.7	9	0%	11.5±1.1	9+1S	10%
ET 1.8 mA	11.8±0.9	10	0%	16.8±0.8	6+4S	40%

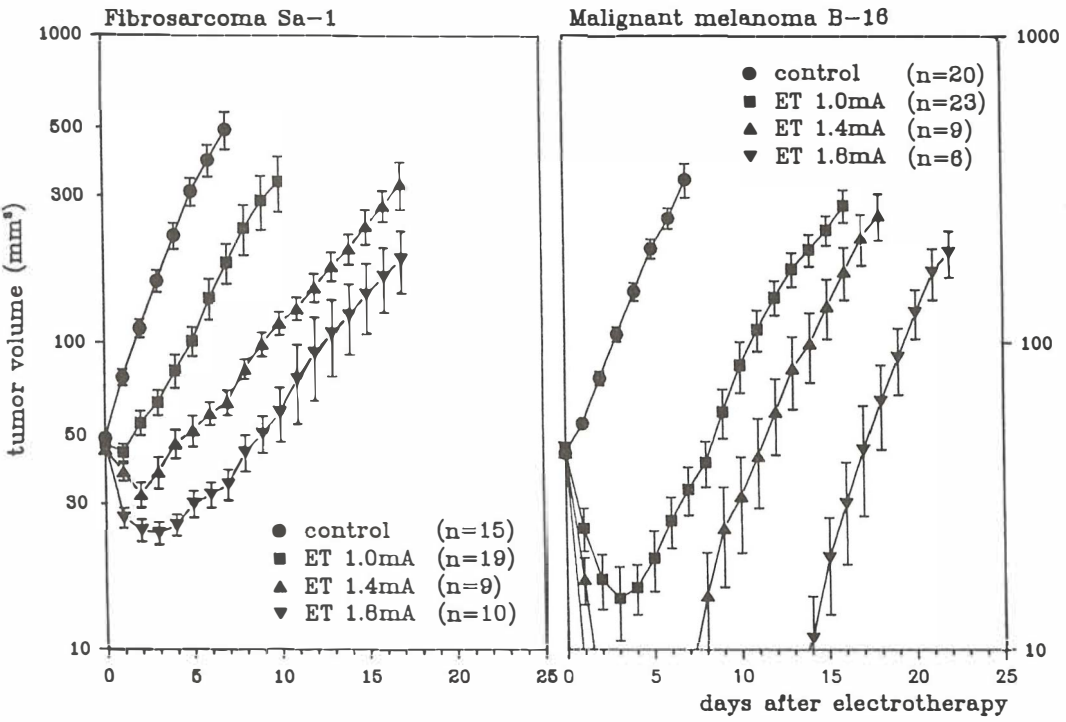

Fig. 1 – Tumor growth curves after single-shot electrotherapy with 1.0, 1.4 and 1.8 mA, one hour duration, for fibrosarcoma Sa-1 (left) and malignant melanoma B-16 (right) murine tumor models. Vertical bars: standard error of the mean.

4. Nordenström BEW. Electrochemical treatment of cancer. I: Variable response to anodic and cathodic fields. Am J Clin Oncol (CCT) 1989; 12: 530-6.

5. Miklavčić D, Serša G, Novaković S, Jerčinović A. Electrical current in treatment of malignant tumors. Trans BRAGS 1990; 10: 55.

6. Miklavčić D, Serša G, Novaković S, Reberšek S. Non-thermal antitumor effect of electrical direct current on murine fibrosarcoma Sa-1 tumor model. In: Brighton CT and Pollack SR eds. Electromagnetics in Biology and Medicine. San Francisco: San Francisco Press, 1991; 222-4.

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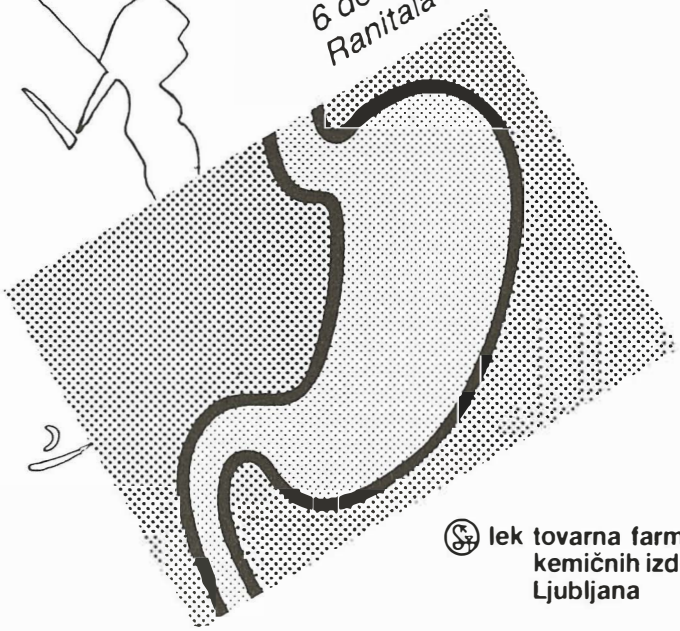

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INŠTITUT ZA DIAGNOSTIČNO IN INTERVENTNO RADIOLOGIJO

KONTRASTNA SREDSTVA PRI SLIKANJU Z MAGNETNO RESONANCO

CONTRAST AGENTS IN MR IMAGING

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Abstract – Basic mechanisms of contrast agents enhancement in MR imaging are presented. The most important chemical compounds, which are contrast carriers such as paramagnetic ions, nitroxides, superparamagnetic and ferromagnetic particles, are described. Their proton relaxivity, stability, toxicity and usability are given.

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Key words: magnetic resonance imaging; contrast media

Letter to editor

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Uvod – Kvaliteta slike je pri slikanju z magnetno resonanco (MR) odvisna od intenzitete merjenega signala. Signal je soodvisen od števila protonov (^1H) in hitrosti relaksacije. Osnovni vir kontrasta v MR sta različna relaksacijska časa posameznih tkiv in razlike v gostoti vode (protonov H). MR sliko dobimo tako, da v močno magnetno polje postavimo vzorec in ga obsevamo z radiofrekvenčnimi (RF) pulzi. Protoni z magnetnimi lastnostmi se v polju usmerijo, RF pulzi pa jih izmaknejo iz ravnovesne lege. T_1 ali longitudinalni oz. spin – mrežni relaksacijski čas je interval, ki ga skupina protonov potrebuje, da se ponovno uredi z magnetnim poljem in se vzpostavi longitudinalna (vzdolžna) magnetizacija. T_2 ali transverzalni oz. spin-spinski relaksacijski čas pove, kako dolgo tkivo zadrži začasno pravokotno magnetizacijo, ki smo jo inducirali z RF pulzom. To je torej čas, ki je potreben, da izgine pravokotna magnetizacija na osnovno zunanje magnetno polje (1). Kontrast slike lahko teoretično spreminjamo s:

I. variacijo parametrov snemanja (poseg v računalniški program)

II. poseganjem v tkiva (v pacienta)

– spreminjanje gostote protonov ^1H (uporaba diuretikov, alkohol, hormoni, dehidracija, veliko vode v GIT...)

– spreminjanje temperature (T_1 je odvisen od temperature zato lahko spreminjamo kontrastnost z ogrevanjem ali ohlajevanjem posameznega dela telesa ali vzorca)

– spreminjanje mangetnega polja (kar dosežemo s kontrastnimi sredstvi (KS).

S KS v MR skrajšamo T_1 in T_2. Kontrasta na sliki dejansko ne vidimo, pač pa je viden le njegov učinek oziroma vpliv KS na magnetno polje vode. V tem se MR KS ločijo od rentgenskih. Tudi uporabne doze so različne. Doze pri MR so od 10^{-5} do 10^{-3} mol/kg, pri rentgenskih jodnih KS pa so doze 10^{-3} do 10^{-2} mol/kg. Tkiva, ki so brez notranjega MR signala ali je šibak, so neprimerna za prikazovanje s KS. To so tkiva z nizko spinsko gostoto, zaradi majhne gostote protonov, kratek T_2 (skelet) ali premikajoči deli (tekoča kri). S povečevanjem koncentracije KS se MR signal ne spreminja linearno in pri večjih koncentracijah KS MR signal povsem izgine (slika 1). Najpomembnejša fizikalna lastnost KS je pozitivna magnetna dovzetnost (magnetna susceptibilnost) (2), ki predstavlja razmerje inducirane magnetizacije proti uporabljenemu polju.

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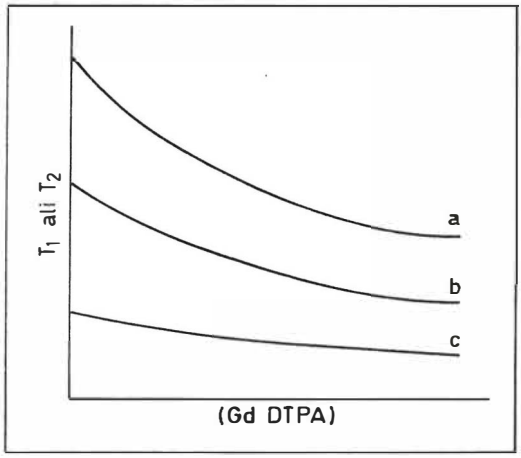


Slika 1 – Vpliv koncentracije Gd–DTPA na spremembe T_1 ali T_2 (a–cerebrospinalna tekočina, b–mišica, c–jetra) (2)

Fig. 1 – Effect of Gd–DTPA concentration on changes in T_1 or T_2 (a–cerebrospinal fluid, b–muscle, c–liver) (2).

Ta vrednost podaja sprejemljivost določene snovi za magnetizacijo z zunanjim magnetnim poljem. Odvisna je od atomske zgradbe in porazdelitve elektronov na orbitalah.

Snovi delimo v diamagnetne, paramagnetne, superparamagnetne in feromagnetne. Diamagnetne snovi imajo negativno magnetno dovzetnost in zato se v njih inducira negativna magnetizacija. Ta efekt je zelo šibak. Večina organskih in anorganskih spojin kaže le diamagnetne lastnosti in so kot take nezanimive kot KS za slikanje z MR.

Princip delovanja kontrastnih sredstev – Značilen za paramagnetne, superparamagnetne in feromagnetne snovi je magnetni učinek nesparjenih elektronskih spinov. Te snovi imajo pozitivno magnetno dovzetnost in zato povzročajo pozitivno inducirano magnetizacijo v magnetnem polju. Magnetni tok okrepi v teh snoveh magnetno polje. Povišana temperatura kvari magnetno urejenost snovi in manjša magnetno dovzetnost. Pri določeni temperaturi (Neelova temperatura) je magnetna dovzetnost enaka nič. Pri spreminjanju magnetnega polja kažejo feromagnetni materiali lastno magnetizacijo, ki ostane tudi po njegovi odstranitvi. Tak magnetni »spomin« se med drugim uporablja za magnetne zapise in za stalne magnete. Superparamagnetne snovi obravnavamo kot termodinamsko neodvisne delce. Njihova magnetna dovzetnost (po atomu ali molu npr. železa) daleč presega odgovarjajoče paramagnetne snovi. Superparamagnetna dovzetnost se linearno veča z močjo polja pri šibkih jakostih in se nasiti (doseže maksimum) pri zadostni jakosti magnetnega polja. Po odstranitivi zunanjega magnetnega polja se inducirana magnetizacija izgubi. Paramagnetna KS vnašamo v organizem kot vodne raztopine, superparamagnetna pa suspendirana. Prva imajo široko uporabnost, druga pa le pri prikazovanju retikuloendotelialnega sistema (RES), kjer izkoriščajo fagocitozo.

Relaksacijski vplivi paramagnetnih snovi so bili prvič opisani leta 1946 (3). Paramagnetizem izhaja iz nesparjenega elektrona, ki tvori magnetno polje in spremeni relaksacijo. Pozitivna magnetna dovzetnost je potrebna, ni pa zadostna za povečanje relaksacije. Večanje relaksacije je odvisno od bližine jedrskih in elektronskih spinov in časa medsebojnega delovanja. Molekuli vode in paramagnetnega KS morata biti zelo blizu, da se prva hitreje relaksira. Različen vpliv na T_1 in T_2 lahko razumemo kot posledico neravnotežja magnetnih momentov, bližine različnih spinov in vpliva faktorja spin/čas. Dogajanja niso popolnoma razjasnjena, čeprav opisujeta naslednji enačbi približne osnove za oblikovanje paramagnetnih KS (4).

$$\frac{1}{T_{1opazovan}} = \frac{1}{T_{1paramagneten}} + \frac{1}{T_{1diamagneten}}$$

$$\frac{1}{T_{2opazovan}} = \frac{1}{T_{2paramagneten}} + \frac{1}{T_{2diamagneten}}$$

$1/T_1$ in $1/T_2$ sta relaksacijski razmerji, opazovani v prisotnosti paramagnetnih molekul. So le vsota proton relaksacijskih razmerij' ki bi se pokazala brez paramagnetne snovi in razmerij, ki so povzročena z vnašanjem le teh. Paramagnetne snovi znižajo T_1 in T_2. Relaksivnost pomeni relativno spremembo relaksacije merjenega vzorca ali tkiva glede na koncentracijo KS (npr. relaksivnost 8 pomeni, da se ob uporabi 1mmol KS poveča relaksacija tkiva za 8-krat).

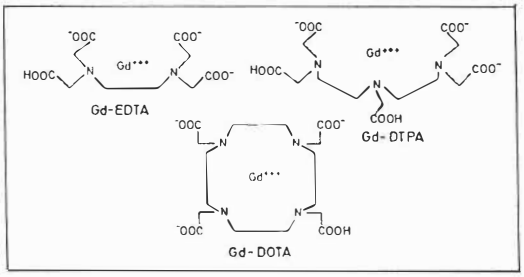
Kot prva KS v MR poglejmo topne paramagnetne snovi (5,6). Določeni kovinski kationi Gd^{+3}, Mn^{+2}, Fe^{+3} in Cr^{+3} so paramagnetni zaradi nesparjenih elektronskih spinov v 3d (prehodne kovine) ali 4f (lantanidi) atomskih orbitalah. Število nesparjenih elektronov je lahko od 0 do 7. Neto molekularni magnetni moment je odvisen od orbitalnega gibanja elektronov in zaščitnega vpliva, ki ga povzroča elektronska vezava v molekularnem povezovanju. Druga bi-

Tabela 1 – Toksičnost različnih paramagnetnih kontrastnih spojin, ki so potencialno zanimive za MR slikanje

Table 2 – Toxicity of several paramagnetic contrast agents which are of potential interest in MR imaging

Spojina Compound	Toksičnost Toxicity (mM/kg)
$MnCl_2$	0,22
$Na_3MnDTPA$	1,9
$Na_2MnEDTA$	7,0
$GdCl_3$	0,26
$Na_2GdDTPA$	20,0

stvena zahteva za KS je visoka toleranca (Tabela 1). Slabo prenašanje Gd^{+3}, Cr^{+3}, Mn^{+2}, Fe^{+3} prostih kovinskih ionov je bil vzrok, da so jih izločili iz proučevanj, čeprav imajo izrazito relaksirajoče delovanje. Učinkovita strategija za zmanjšanje toksičnosti, pri tem pa se ohrani paramagnetni učinek, je keliranje ionov z makrocikličnimi ligandi (slika 2). S tem se onemogoči možnost vezave ionov na biološka vezna mesta. Keliranje zmanjša toksičnost, vpliva na biodistribucijo, stabilnost in izločanje. Stabilnost kompleksov predstavlja kritičen podatek za toksično delovanje. Gd^{+3}–ion je v Gd–DTPA tesno pripet s termodinamsko stabilnostno konstanto $K_s = 10^{23}$, v DOTA pa še močneje, $K_s = 10^{28}$, kar rezultira v višji letalni dozi. Keliranje kovine spremeni njeno obnašanje. Pristop molekul topila do kovinskega iona je zmanjšan, upočasni se njegovo gibanje, čuti se vpliv liganda na relaksacijo.



Slika 2 – Strukturne formule Gd–kelatov

Fig. 2 – Structural formules of Gd–chelates

Lantanidi – Uporabnost lantanidov se je pokazala šele pri razvoju MR KS. Močno skrajšajo relaksacijske čase. Gd^{+3} in Eu^{+2} imata sedem nesparjenih elektronov in najvišje spinsko kvantno število. Gd^{+3} ima od vseh proučevanih paramagnetnih snovi največji relaksacijski učinek. Keliranje lantanidov spremeni relaksivnost in toksičnost. Lantanidi imajo veliko afiniteto vezave z poliaminopolikarboksilnimi kislinami. Testirajo dietilentriaminpentaocetno kislino (DTPA), ki se je že uporabljala kot antidot pri zastrupitvah z lantanidi. Gd^{+3} kaže največjo protonsko relaksacijo pri vezavi v makromolekularne komplekse z aminokarboksilnimi kislinami, derivati albumina, imunoglobulini ali biokompatibilnimi polimeri. Lantanidov v telesu sesalcev normalno ni. Prosti lantanidi so v dozah od 10 do 20 μmol/kg močno hepatotoksični. Pojavijo se maščobne degeneracije jeter in fokalne nekroze že po 12 urah. Pri poskusih in vitro povzroče nizke doze lantanidov precipitacijo nukleinskih kislin, inhibirajo RNA polimerazo, jetrno lipoproteinsko mobilizacijo, glukoneogenezo, tvorijo efekte kalcijevega antagonizma, stimulirajo sproščanje nadledvičnih kateholaminov in nadomeščajo kalcij v encimih, ki vsebujejo kovino (metaloencimi) in s tem spremene njihovo aktivnost. Znanih je nekaj Gd^{+3} izredno stabilnih kompleksov, ki se tudi zadovoljivo izločajo iz organizma: Gd-DTPA, Gd-CDTA (cikloheksandiamintetraocetna kislina) in Gd-DOTA (tetraciklododekantetraocetna kislina). So anionski kelati, ki se nespecifično porazdelijo ekstracelularno in izločijo z glomerularno filtracijo. Normalno ne prestopijo hemato-encefalne bariere. Za razliko od prostih kovin in manj stabilnih kelatov se v uporabljanih dozah dobro prenašajo. Gd-DTPA dimeglumin je prvo klinično testirano parenteralno KS za MR (7) in junija 1988 registrirano pri Food and Drug Administration (FDA) v ZDA. Dosegljiv je pod zaščitenim imenom Magnevist^R (Schering). Reverzibilni stranski učinki Gd-DTPA so hipotenzija, dvig serumskega železa (pri 15 do 30% pacientih, vzrok je neznan) in pojav nenormalnih jetrnih funkcijskih testov z dvigom bilirubina (pri 2% pacientov, mehanizem neznan).

Druge spojine gadolinija kažejo predvsem afiniteto do RES in hepatobiliarnega sistema. Gd-oksidi in hidroksidi so pri fiziološkem pH-ju netopni in se lahko oblikujejo kot suspenzije. Nekateri Gd-kompleksi kot npr. Gd-iminodiacetati se večinoma pojavijo v hepatobiliarnem sistemu in izločijo preko biliarnih poti (8). Ostali lantanidi so bili zaradi izredne toksičnosti manj testirani, čeprav imajo nekateri večji magnetni moment.

Prehodne kovine – so močno relaksirajoči elementi. Sem sodijo posebno Mn^{+2}, Cr^{+3} in Fe^{+3} z nesparjenimi elektroni. Omenjeni elementi so prisotni tudi v biomolekulah. Mn^{+2} je odličen relaksirajoč element z najdaljšim elektronspinskim relaksacijskim časom med prehodnimi kovi-

nami. $MnCl_2$ povzroči takojšnjo hepatobiliarno relaksacijo, ki pojenja šele po več urah. Mehanizem te nenavadne poti izločanja je neznan. Nekateri Mn-kelati kot npr Mn-PDTA (mangan–propanodiaminotetraocetna kislina) in Mn-EGTA (mangan–etilenglikolaminoetiletertetraocetna kislina) kažejo podobno afiniteto do hepatobiliarnega sistema (9).Vnešeni manganovi kompleksi se v telesu metabolizirajo, metaboliti še niso popolnoma znani. Verjetno se Mn^{+2} v krvnem obtoku veže z makromolekulami. Prost Mn^{+2} je strupen. $MnCl_2$ v večjih dozah kot 10 μmol/kg je kardiovaskularno toksičen zaradi blokade kalcija. Pojavijo se spremembe v EKG zapisu (QT in PR interval se podaljšata), pojavi se povišan krvni tlak in lahko tudi ventrikularna fibrilacija, tahikardija ali bradikardija pri dozi 0,2 mmol/kg.

Cr^{+3} so proučevali v kompleksu z EDTA, kot prost pa je strupen. V skupini prehodnih kovin so obetavni kontrasti z železom. Železove spojine vsebujejo nevrtralno železo (Fe), ione v feri (Fe^{+3}) ali fero (Fe^{+2}) obliki. Feri in fero spojine vsebujejo štiri ali pet 3d orbitalnih elektronov, ki se obnašajo paramagnetno ali superparamagnetno. Železo je normalno prisotno v telesu (1 mmol/kg), njegov metabolizem je dobro poznan. Nahaja se v eritrocitih, kostnem mozgu, RES-u in mišicah, kjer je vezano na funkcionalne proteine (hemoglobin, mioglobin, hem– ali nehem–encime, transportne proteine – transferin,...). Glavna biološka naloga železa so redoks reakcije v transportu kisika in elektronov. Znane so tudi zastrupitve z železom. Posebno so pogoste akutne zastrupitve pri otrocih pri peroralnem vnosu večjih količin zdravil z železom. Pojavijo se gastrointestinalne (GIT) motnje, hepatična in srčna nekroza. Opisana je celo smrt že pri nizki peroralni dozi (2 mmol/kg). Parenteralno vnešeno prosto železo je toksično še v nižjih koncentracijah. Doze parenteralno vnešenega železa 2 mmol Fe/dan kot železo z dekstranom lahko povzroče lokalno bolečino, limfadenitis, glavobol, slabost, vročino, urtikarijo, artralgijo, mialgijo, hipotenzijo in redko anafilaksijo. KS v MR vsebujejo železo v obliki soli za peroralno uporabo (za prikaz GIT) in v obliki stabilnih kelatov za parenteralno. Prva uporabljena Fe–sol je bil $FeCl_3$, vendar ni ustrezal, ker draži GIT, boljši je železo–amonijevcitrat. Lepo prikaže proksimalni del GIT, v distalnem pa je efekt slabši, ker verjetno pride do razredčitve in redukcije spojine (10). Železov kompleks Ferrioxamin B uporabljajo za prikazovanje sečnih poti, je pa kardiovaskularno toksičen in kot tak nevaren. Obetavna sta železova fenolata, Fe–EHPG (etilenhidroksifenilglicin) in Fe–HBED (hidroksibenziletilendiamin), ki se izločata hepatobiliarno (11,12). Fe–HBED je najstabilnejši železov kelat, ki povzroči takojšnje hepatobiliarno obarvanje in obarvanje sečnih poti pri T_1 obteženih slikah MR.

Superparamagnetni železov oksid apliciran subkutano se zbira v bezgavkah in predstavlja KS za MR limfografijo (13).

Nitroksili – Nitroksili so organski radikali z vsaj enim nesparjenim elektronom. Pred razvojem MR so jih uporabljali kot paramagnetne snovi v biokemiji. Organski prosti radikali so relativno malo toksični. V organizmu se metabolizirajo po oksidacijsko–redukcijskem encimskem mehanizmu v hidroksilamine, ki pa niso paramagnetni. Hitrost redukcije je višja v hipoksičnih celicah, kar se lahko izkorišča za merjenje intracelularnega nivoja kisika (14). Farmakološka proučevanja vključujejo vrednotenje farmakokinetičnih parametrov. Možno jih je modificirati s kemijsko sintezo. Relaksacijski učinki nitroksilov se povečajo s povečanjem molekulske mase, s proteinsko bogatim okoljem, šibkejšim magnetnim poljem, z uvedbo alkoholnih ali amidnih skupin. Večji efekt imajo nitroksili piridinskega tipa, piperidinski pa so v organizmu stabilnejši. V primerjavi s kovinskimi paramagnetnimi spojinami so nitroksili znatno šibkejši, vendar imajo najdaljši elektron–spinski relaksacijski čas. Iz tega sledi, da imajo makromolekularni konjugati nitroksilov s proteini, maščobnimi kislinami ali aminokislinami upočasnjeno molekularno gibanje in s tem izboljšano relaksivnost (ca. 10–krat) (15,16). Za povečanje učinkovitosti in varnosti nitroksilov kot KS v MR potekajo intenzivne raziskave. Posebno pozornost zasluži dejstvo, da bi nitroksile potencialno lahko uporabili kot indikatorje metabolične aktivnosti organizma (14). Jasno je, da prosti radikali okvarjajo DNA, ni pa podatkov, ki bi pripisovali nitroksilom mutageno ali kancerogeno delovanje.

Tehnološke možnosti – Oblikovanje KS za MR vključuje vgrajevanje paramagnetnih (Gd–DTPA, Mn^{+2}–kelatov,...), superparamagnetnih ali feromagnetnih spojin v liposome ali koloidno disperzne sisteme (17). Ti so se izkazali zelo uporabni za prikazovanje RES-a, ker se liposomi z vgrajenim manganom kopičijo izključno v RES s fagocitozo. Hkrati se pokažejo tudi jetra (Kupferjeve celice). Uporaba gadolinijevega oksida je v teh oblikah omejena zaradi njegovega hepatotoksičnega delovanja (subakutni multifokalni hepatitis). Superparamagnetne in feromagnetne spojine v RES-u zmanjšajo intenzivnost

signala, kar privede do bistvenega skrajšanja T_2 in se tako razlikujejo od učinkovanja topnih paramagnetnih snovi. Zaradi zmanjšanja signala organ na sliki ni več viden. Patološko spremenjeno tkivo obdrži svoj signal in je zaradi večje kontrastnosti bistveno bolj vidno. Glavni problem je dolgo zadrževanje teh oblik kontrasta v RES, za kar so potrebna dodatna klinična testiranja.

Ciljana kontrastna sredstva – Ciljana kontrastna sredstva predstavljajo KS za specifično področje organizma. Pristop je podoben kot pri protitelesih označenih z radioindikatorjem v scintigrafiji. Poslužujejo se konjugiranja specifičnih proteinov z DTPA in paramagnetnim ionom. Zaradi upočasnjega rotacijskega gibanja kompleksa se poveča relaksivnost in obdrži imunoreaktivnost (18). Pri biološkem testiranju so dokazali pojav preobčutljivosti, kar omejuje uporabnost teh kompleksov. Pri označevanju protiteles z železom nastopi prevelika obremenitev organizma z železom.

Raziskujejo tudi druge snovi kot so iskalci tumorjev (porfirini) in intravaskularni označevalci. Pomanjkljivosti le teh je njihova akutna toksičnost.

Zaključek – V članku je opisan osnovni mehanizem delovanja KS v MR. Povdarjene so najvažnejše kemične skupine, ki so nosilci kontrasta: paramagnetni ioni, nitroksili, superparamagnetni in feromagnetni delci. Predstavljene so glede na protonsko relaksivnost, stabilnost, toksičnost in uporabnost v MR slikanju.

Literatura

1. Schild HH. MRI made easy. Berlin: Schering AG, 1990.
2. Stark DD, Bradley WG. Magnetic resonance imaging. New York: Mosbey Company, 1988.
3. Bloch F, Hansen WW, Packard P. The nuclear induction experiment. Physiol Rev 1946; 70: 474-85.
4. Bertini I, Luchinat JD. NMR of paramagnetic molecules. Menlo Park. CA: Benjamin/cammings, 1986.
5. Lauterbur PC, Menodsa–Dias RH, Rudin AM. Augmentation of tissue water proton spin lattice relaxation rates ty in vivo addition of paramagnetic ions. In: Dutton PL, Leigh JS, Scarpa A. Frontiers of biological energetics. New York: 1978.
6. Bačić G. MRI kontrasti: mehanizam dejstva i primena. Farm vestn 1990;41:280-85.
7. Brasch RC. Principles of MRI contrast enhancement. In: Budinger TF, Margulis AR. Medical Magnetic Resonance. Society of Magnetic Resonance in Medicine, 1988, 121-8.
8. Lauffer RB. Paramagnetic metal complexes as water proton relaxation agents for NMR imaging: theory and design. Chem Rev 1987;87:901-27.
9. Spiller M, Browen RD, Koening SH et al. The state of Mn^{+2} in liver bile and blood after iv injection or infusion of Mn^{+2} chelates in rabbits investigated using the field dependence of $1/T_1$. Soc Magn Res Med 1986;25-6.
10. Wesbey GE, Brasch RC, Goldberg HI et al. Clinical experience with dilute oral iron solutions used for GIT contrast emhancement in abdominal NMR imaging. Mag Reson Imaging 1958;3:57-64.
11. Engelstad BL, Ramos EC, Macapinlac HA et al. Fe–HBED and Fe–EHPG iron complexes exhibiting hepatobiliary enhancement in MRI. Clin Nucl Med 1986;11:19.
12. Renshaw PF, Owen CS, Mc Laughline AC et al. Feromagnetic contrast agents: a new approach. Magn Reson Med 1986;3:217-25.
13. Saini S, Modic MT, Hamm B, Hahn PF. Advances in contrast–enhanced MR imaging. AJR 1991; 156:235-9.
14. Demšar F, Kveder M, Rugelj S et al. Hydroxylamines as oxygensensitive procontrast agents for in vivo MRI. J Magn Reson 1991;95: in press.
15. Lovin JD, Wesbey GE, Engelstad BL et al. Structure–relaxivity relationships for sixteen nitroxide spin labels potentially suit able as NMR contrast agents. Magn Reson Imaging 1985;3:73-81.
16. Ehman LR, Brasch RC, McNamara MT et al. Diradical nitroxyl spin label contrast agents for magnetic resonance imaging. A comparison of relaxation effectiveness. Invest Radiol 1986; 21:125-31.
17. Unger E, Needleman P, Cullis P, Tilcock C. Gadolinium–DTPA liposo mes as a potential MRI contrast agent. Invest Radiol 1988; 23:928-32.
18. Schrere P, Aisen AM. Monoclonal antibodies labeled with polymeric paramagnetic ion chelates. Magn Reson Med 1986; 34:336-40.

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DOSE IN RADIOTHERAPY

ESTRO–IAEA SEMINAR, SEPTEMBER 16-21, 1991, LEUVEN

In September 1991 a seminar on »Radiation Dose in Radiotherapy: from Prescription to Delivery« was organized in Leuven /Belgium by ESTRO (European Society for Therapeutic Radiology and Oncology) under the auspices of IAEA (International Agency for Atomic Energy) from Vienna.

The seminar was aimed to analyse all the steps taken in radiation treeatment procedures, and thus ensure that the prescribed doses are delivered to irradiation field as scheduled. Among the participants there were over 90 radiophysicists from Europe, U.S.A., Middle East and Africa, and a few invited speakers whose lectures represented the basis of the seminar.

Day 1 program comprised a series of presentations on general questions such as e.g. the degree of accuracy required in radiotherapy, the need for Quality Assurance Program etc. Individual stages in a radiation procedure that contribute to dosimetric and geometric were grouped as follows:

1. dosimetry
2. patient's data and parameters
3. dose planning
4. beam set–up
5. patient set–up
6. irradiation

The degree of accuracy in dosimetry should be determined by SD (standard deviation) for the probability of tumour control, which should not exceed 10% (H.K. Awwad, Cairo). If all the steps in treatment procedure are carried out correctly, 5% accuracy in dose determination with 3% SD can be achieved. A high SD in the dose distribution in target volume is believed to be less dangerous that a high SD in the mean tumour dose. The ICRU Report No. 29 standardizing the reports on dose determination in radiotherapy was discussed in detail. As the document dates back to the year 1978, it needs to be updated in accordance with progress in dosimetry, expanding use at computers in radiotherapy and some other comments concerning its contents (T. Landberg, Malmö).

Day 2 of the seminar was dedicated to the calibration of dosimeters and radiation as well as to radiation beam characteristics.

E. Swensson (IAEA, Vienna) represented a net of substandard laboratories which would enable users to have their dosimeters calibration with the referential standard in Paris. IAEA Protocol (Technical Report No. 277) should be accepted as a uniform standard for the determination of photon and electron doses worldwide.

Special attention has been paid to the quality assurance (QA). Thus every radiotherapy center should have a QA program adjusted to their own needs.

K.A. Johansson reported on the study results obtained by a group of radiophysicists from Gothenburg. Within the program of this study, TLD dosimeters were sent to several radiotherapy centers in Europe and elsewhere in order to be irradiated under referential conditions with a dose of 100 cGy. Afterwards, actual doses received by dosimeters were determined. In the period from 1968 to 1984, the measurements were repeated three times and 330 sources of X–rays, Co–60 and electrons were compared. It has been established that during the investigation period the number of measured x–ray and electron doses deviating from the referential values for less than 3% increased from 50% to 98%. For Co-60 photon beam this rate was 100% throughout the observation period. Among the participating institutions was also the Institute of Oncology in Ljubljana, where a sufficiently accurate calibration of machines has been established (<3% deviation).

One of the two main topics that were discussed on **Day 3** were patient's data and parameters needed in treatment planning. In her excellent lecture J. Dobbs (London) pointed out the advantages and drawback of individual methods for data collecting, i.e. mechanical plotters of countu-

res radiological examinations, computed tomography (CT) and magnetic resonance (MR). In the view of accurate treatment planning, CT has become practically indispensable as it provides reliable data on the exact position and density of individual body structures. though diagnostic value of MR images is indisputable, the method has proved useless in dosimetry since it does not give data on tissue density, and the obtained images are geometrically distorted.

A. Dutreix held an interesting lecture on the importance of tissue heterogeneity consideration in treatment planning. The second topic dealt with dosimetry in vivo. There, termoluminiscent dosimetry and semiconductor diodes were presented in detail. Two novelties in this field, i.e. dose determination from portal images and dosimetry by means of alanine were mentioned. Alanine uptake in the cells occurs under the influence of and it's concentration in the cell is dose dependent. It can be determined by ESR (electron spin resonance), thus providing the data on cumulative dose received by the irradiated tissue before measurement.

The guideline of the seminar was QA in radiotherapy at all stages of the procedure, and therefore the whole **Day 4** program was dedicated to this topic. Quality audit is performed by different study groups of radiophysicists as well as by institutions. As the basic dosimetry in radiotherapy is relatively advanced, they also test the quality of other factors such as e.g. treatment planning systems. For this purpose, different phantoms with built–in heterogeneities, breast phantom, RANDO phantom etc., intended for *in vivo* quality testing of dosimetric procedures, are used. According to the results of these studies, inaccuracy of the dose in the reference point of irradiated volume is relatively small (< 1-2%), whereas outside that point it can increase significantly in certain cases (in breast irradiation to >10%). This error is further enhanced by computed treatment planning programs where the heterogeneity of structures is frequently considered incorrectly in dose calculating.

The last day was dedicated to portal imaging. S. Faermann and Y. Krutman developed a physical model of a cassette for gammagraphy. B.J. Mijnheer (Amsterdam) presented a series of new portal imaging techniques where image is created on a matrix–ionization chamber or on a fluorescent screen placed underneath the patient during irradiation. The image is available on computer screen only a few seconds after the procedure. Recently, new systems are being developed which provide real time images that can be compared with simulator images of the same irradiation field on the screen. This represents one of the greatest achievements in the endeavours for radiotherapy improvement.

The seminar was characterised by relaxed atmosphere and lively discussion. The participants from developing countries showed unexpectedly sound knowledge and ambition to solve problems in radiotherapy. Though QA in this field of medicine largely depends on the available material basis, knowledge, accuracy and experience as well as the supervision of equipment and procedures are believed to be of major importance.

Bogdan Umek, M.Sc.
The Institute of Oncology Ljubljana

ESTRO TEACHING COURSE OF BASIC CLINICAL RADIOBIOLOGY

October 5-9, 1991, Athens

ESTRO in collaboration with the University of Athens organized and successfully performed a 5-day course on clinical aspects of radiobiology. Lectures were held in the outskirts of Athens, in Vouliagmeni, which provided stimulating environment for work.

The list of teaching staff (G.G. Steel, A.C. Begg, M.C. Joiner, J. Overgaard, A. van den Kogel) promised a high level of lectures, and these expectations have been completely fulfilled.

In the series of lectures which lasted throughout the working day »classical« radiobiological topics such as 5-R, cell kinetics and proliferation, radiobiology of tissues etc. were discussed first. There were tutorials held between the lectures, which offered excellent opportunities for informal chat with lecturers by the pool with a cup of coffee. More »recent« topics such as LQ model, unconventional fractionation, hyperthermia, photodynamic therapy, flow cytometry, interaction of radiation with chemotherapy etc., were also covered in sufficient detail, so the course can be regarded as an excellent »high school« of radiobiology for clinicians.

The organization and especially the academic level of lecturers and their presentations were of the highest standard.

Boris Jančar, MD
The Institute of Oncology, Ljubljana

CANCER IN ORGAN TRANSPLANT RECIPIENTS

Edited by Dietrich Schmähl and Israel Penn. 183 pp., illustrated, 21 figures. Springer–Verlag, Berlin Heidelberg New York, 1991.

The book presents a detailed analysis of the problem of cancers that occur before and after organ transplantation.

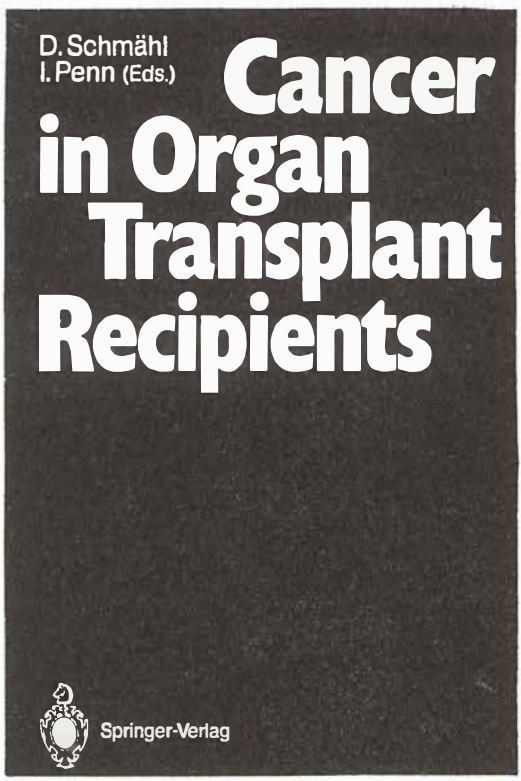
As noted in the preface, in 1968 T.E. Starzl and I. Penn from Denver recognized that a cancer *de novo* could develop after transplantations. They observed two lymphomas: one was a non–Hodgkin lymphoma involving the stomach and other organs, and the second a multifocal non–Hodgkin lymphoma of the brain. This experience stimulated inquiries at other transplant centers and resulted in reports of another three cases. That was the beginning and reason for studying of cancer after organ transplantation.

At the 1968 Summer Meeting of the Transplantation Society in New York it was suggested that Dr. Penn should start a registry to collect data on post-transplant malignancies. This led to the establishment of Denver (now Cincinnati) Transplant Tumor Registry, which collected data from transplant centers throughout the world, and which has provided numerous publications on the subject. Many investigators at other transplant centers have also published data concerning experience with these tumors, gained at their own centers, or gleaned from regional registries. Some of them are contributors in the debated book.

Another group of tumors occurring in transplant patients, that is discussed in this book too, comprises neoplasms that involve a vital organ; the only effective treatment is removal of the entire organ and its replacement with a healthy one, in other words, transplantation. But a fundamental question that arises is: if any residual tumor cells are left behind, how do they behave when the patient's immune defenses are impaired by immunosuppressive therapy? These are some of the questions discussed in this book.

In the summer of 1989 Prof. D. Schmähl conceived the idea of inviting a small group of experts in various fields – basic cancer research, molecular biology, epidemiology, oncology, virology, nephrology, immunology, pathology, and transplantation surgery – to meet for two days for a »brainstorming« session to discuss in depth the field of (1) *de novo* malignancies after transplantations, and (2) the treatment of pre-existing cancers by organ transplantations. Together with Dr. I. Penn they prepared the program and list of invited speakers. The brain storming session was held in May, 1990 in Heidelberg in the Federal Republic of Germany. This book is the outcome of the presentations and discussions of all the papers.

This would be all, as to a brief history of the book. The book is undoubtedly impressive in contents and scope.



The list of contributors comprises authors from around the world; they have published a number of articles in the world literature in the past years, thus, the book is quite up to date.

The publication is well organized and distributed in four sections:

The first one is centred on the analysis of ***de novo* cancer in organ transplant patients.** It has been pointed out that differences in tumor incidences and tumor patterns in post–transplant patients between various transplantation centers depend on the degree of immunosuppression, the combination of immunosuppressive agent with other drugs, the kind of organ transplantation, as well as on the treatment and diseases that the patients had before transplantation.

Part two addresses **The treatment of cancer by organ transplantation** and comprehends *Liver transplantation for malignant disease, Bone marrow transplantation, and Transplantation of the upper gastrointestinal organs.* Within the above field of problems it has been marked that for symptomatic *kidney* cancers tumor recurrence rates indicate that it is advisable to wait at least 24 months after primary therapy before performing the transplantation, otherwise a dramatic increase in tumor recurrence rates can be expected. For incidentally discovered renal tumors the prognosis is much better. In these cases, it is not necessary to wait until two years have passed, transplantation may be performed as soon as possible.

Part three focuses on **Possible causes of cancer in transplant patients.** It has been emphasized that multiple factors probably play a role in the etiology of the various cancers that occur post-transplantation. Immunodeficiency *per se* and infection with oncogenic viruses are probably the major influences. There was discussed their role and also those of the underlying diseases requiring transplantations; direct damage to DNA by various immunosuppressive treatments; possible synergistic effect of these treatments with various carcinogens; and genetic factors influencing susceptibility or resistance to the development of malignancy.

Part four reviews **A possible prevention of *de novo* cancer in transplant patients.** It has been stated that clinical measures such as maintaining immunosuppressive levels as low as is possibly compatible with graft survival, reducing exposure to sunlight, and ensuring antiviral prophylaxis have limited value. Apart from the vaccine against hepatitis B, it seems to be far away from developing effective vaccines against other potentially oncogenic viruses. The impeding introduction of variety of new immunosuppressive agents and a host of new monoclonal antibodies is unlikely to reduce the incidence of post–transplant malignancies as long as their effects involve suppression of the host's immune defences. The authors believe our research must becentred on inducing specific immunologic unresponsiveness directed only against the foreign antigens of the graft, but leaving intact immune responses to all types of infectious agents and to nascent malignancies.

The most relevant chapters of this book are Discussions at the end of each section of the book. The pointing out and accents in these chapters are the most interesting.

The figures and tables in each chapter are well done and helpful.

Unlike most multiauthored works, it has surprisingly little variation in the excellent quality and clarity of its writing.

The book can be recommended unequivocally as a thoughtful and stimulating appraisal of *de novo* cancer in transplant patients.

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2. Chapman S, Nakielny R. A guide to radiological procedures. London: Bailliere Tindall, 1986.

3. Evans R, Alexander P. Mechanisms of extracellular kiling of nucleated mammalian cells by macrophages. In: Nelson DS ed. Immunobiology of macrophage. New York: Academic Press, 1976; 45–74.

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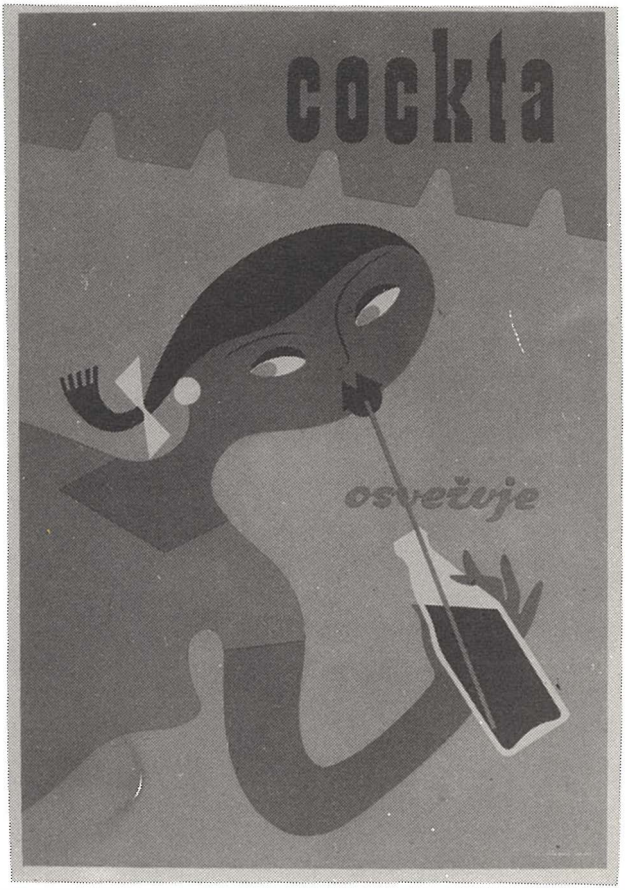

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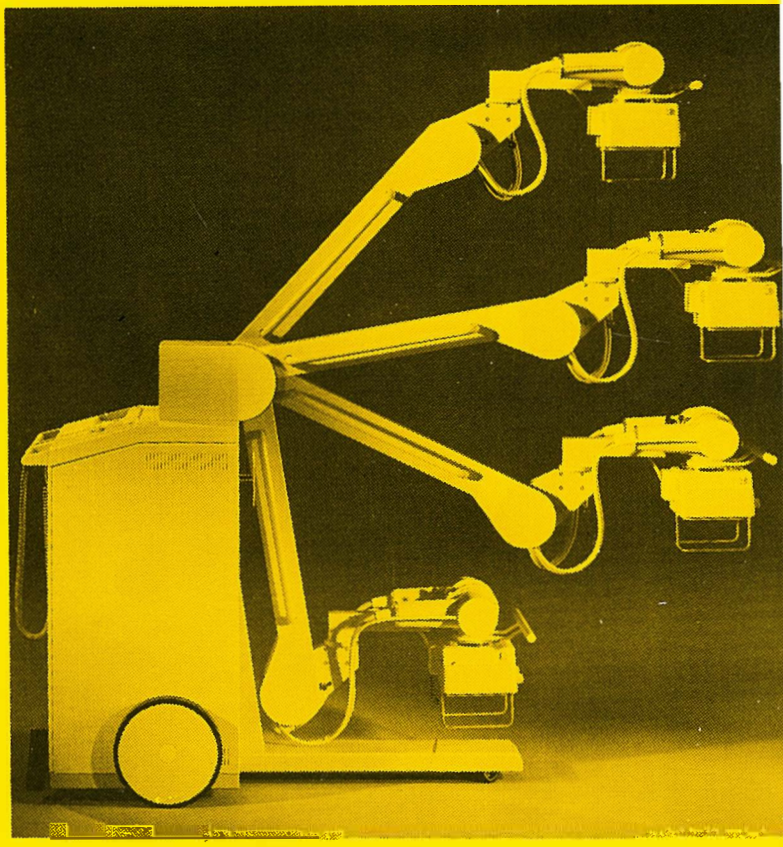

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