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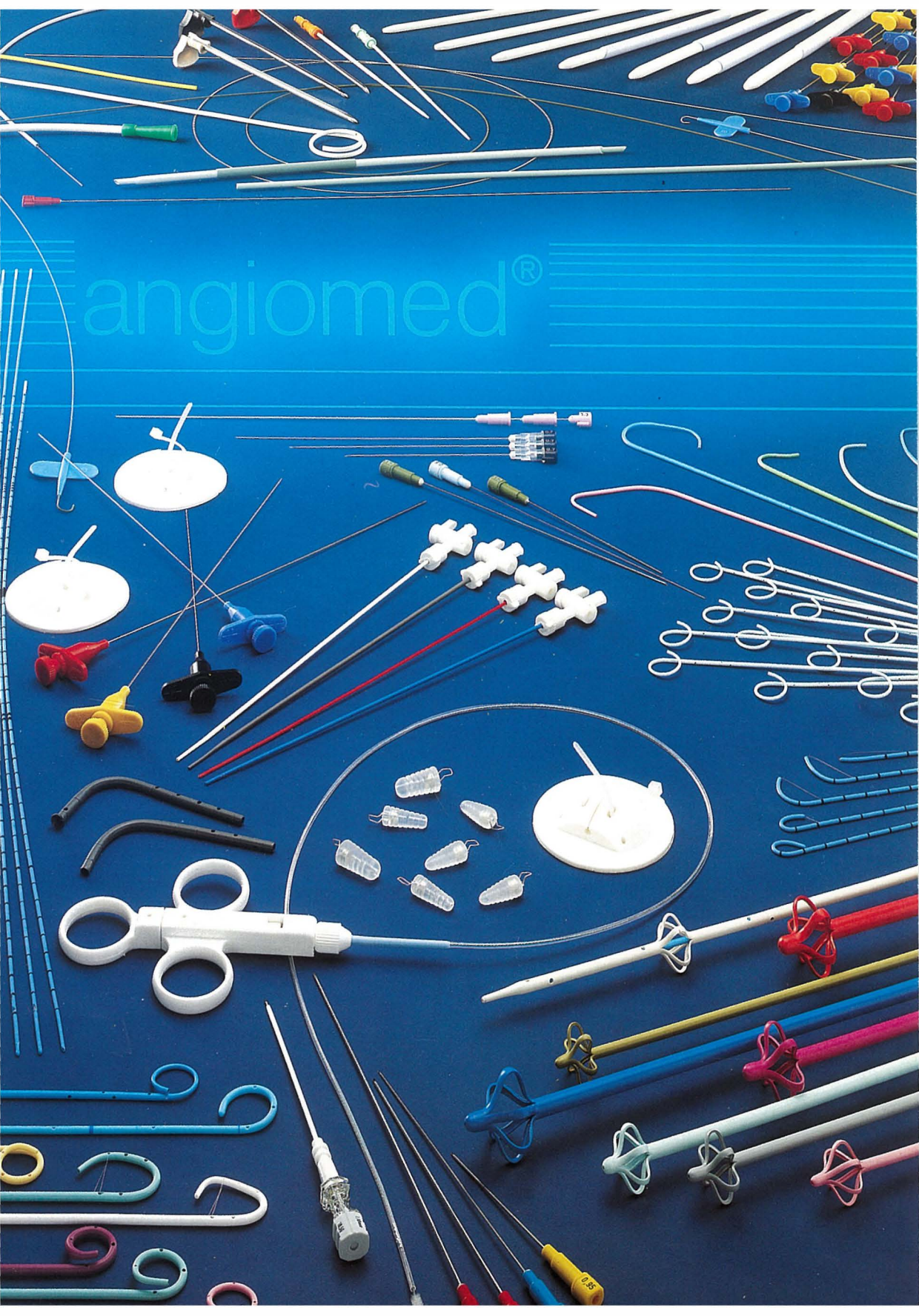
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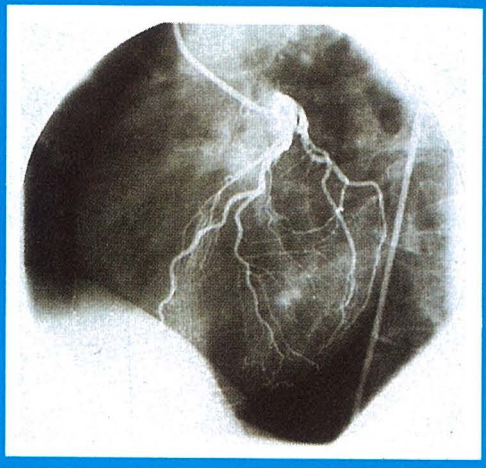

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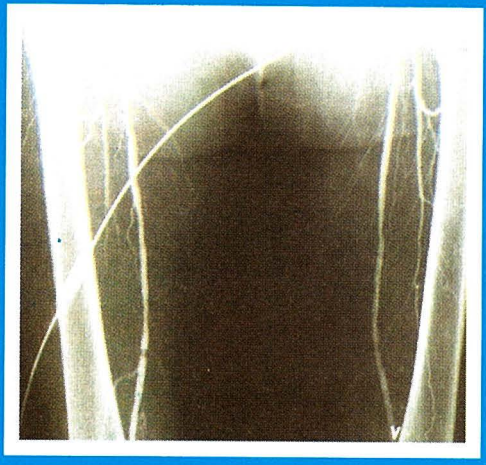

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Dear Readers and Authors,

We dare say that the present No. 3/91 represents an important advance in our radiologic and nuclear medical publishing. All until few years back, RADIOLOGIA IUGOSLAVICA had been a mere reflection of the existing situation in our scientific and professional work. Aimed to put a stop to such practice, this issue published exclusively in English is in a way ahead of our reality, thus indicating the direction in further development of the specific branches of medicine covered by our journal.

According to the policy of our Editorial Board, preference is given primarily to the pubblication of original scientific and review papers that could prove valuable so in daily clinical practice as well as in the education of professionals. We also continuously strive to expand the circle of our regular coworkers, particularly foreign authors, with the intention to attract a larger number of readers and subscribers from abroad. The journal in the present form is therefore designed not to be ours alone, but to be, hopefully, accepted by a broader European reading public. We believe that such a concept is justified also by the present poiitical and economic situation in Yugoslavia; the near generalized war–like conditions threaten to severely affect the country's economy as well as our health care and research activities. The first results of such negative tendencies have already become apparent: Thus, the number of papers submitted for publication to our journal is daily decreasing, and so is also the number of our subscribers. Apart from that, it has become increasingly difficult to secure the financial means needed for regular publication. Now, it appears that it is up to us – physicians and researchers, whose mission reaches beyond these present difficulties – to strive for the international recognition and quality of our journal, and to ensure its regular publication.

The editorial work on the jubilee issue dedicated to the 25th volume of Radiologia lugoslavica is proceeding as planned. The papers are being reviewed and proof–read. Essential corrections are done in collaboration with authors whenever necessary. Here it should be pointed out that we greatly appreciate such cooperation, and therefore all the participating individuals and institutions are kindly asked to stay by our side till the publication is finally ready. I am convinced our mutual efforts will be rewarded by a fair share of pride and satisfaction at a successful outcome.

The coverage of articles reporting on the latest advances and confronting ideas in the appointed fields of medicine should be of interest to a wide circle of readers.

On behalf of our journal Radiologia lugoslavica, I wish to our present and potential coworkers a lot of success in their work.

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PERCUTANEOUS TRANSLUMINAL ANGIOPLASTY: THERAPEUTIC TREATMENT CONCERNING ARTERIOVENOUS FISTULA COMPLICATIONS IN HEMODIALYSIS

Tkalec V, Fedel V, Jerin L, Pikot D, Fedel I

Abstract – Ten patients on regular hemodialysis with arteriovenous fistula complications have been treated by percutaneous transluminal angioplasty (PTA) at Dialysis Center Pula, in the period from October 1986 to October 1990. From 1986 the color Doppler sonography has been combined with angiography in the diagnosis of AV fistula complications when PTA is planned. There were 31 combined examinations performed in 26 patients, the findings revealed 13 cases of arteriovenous fistula thrombosis, 8 venous stenoses exceeding 8 cm or multiple stenoses. Proximal radial artery stenoses were found in 3 cases, anastomotic venous stenosis in 2 and venous limb stenosis shorter than 4 cm in 5 cases. A dilatation technique with PTA balloon catheter is described. Due to the high stenotic resistance (severe fibrosis), balloon inflation pressure of 8 to 12 atmospheres was used. Duration of inflation pressure was up to 2 minutes and was repeated 10 times. The criteria of successful PTA is dialysis duration of the same fistula after treatment, which should be at least 6 months at an adequate flow rate. Out of 10 fistulas treated with PTA, only one artery and one venous stenosis ceased to function after 2 weeks and 1 month respectively from the treatment. The PTA treatment was successful in 4 venous stenoses, 2 artery stenoses and in an anastomotic stenosis. PTA is the treatment of choice in venous (limb) stenosis not exceeding 4 cm. Other complications should be treated surgically.

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Key words: hemodialysis–adverse effects; arteriovenous fistula; angioplasty, transluminal;

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Radiol Iugosl 1991; 25:185-92.

Introduction – A chronic terminal renal insufficiency can be treated by regular dialysis or kidney transplantation. For an adequate hemodialysis at least 300 ml/min blood flow is needed. An adequate vascular approach ensures such flow rate. Radiocephalic arteriovenous fistula on the distal forearm of the nondominant arm is the site of choice in a vascular access to the regular dialysis (1, 2). This type of fistula remains patent in 80 – 90 % of patients, for a period of two years (3). The number of suitable sites for vascular access is limited, and therefore, it is important to maintain each fistula function for as long as possible. An AV fistula can undergo a lot of complications due to various reasons. The demand for a long–lasting fistula function and prevention of complications requires a perfect choice of the site, an evaluation of the vessel quality and a proper technique of fistula construction. The evaluation of the vascular tree is done by means of noninvasive methods: physical examination of the extremities and color Doppler sonography. Color Doppler sonography as a noninvasive and reliable, method has been preferred over all other examination techniques (2, 4). Color Doppler spectral blood flow analysis gives a very good and accurate image of the arterial and venous tree condition, and all pathological processes and complications of arteries and veins can be found. Regarding its qualities, we use the Doppler technique in combination with angiography to diagnose AV fistula complications (4, 5). Color Doppler sonography of the arterial and venous circulation, photoplethysmography and plethysmography give significant information on the blood vessels and the methods should be used as a complementary method to angiography (2, 4) to diagnose AV fistula complications. In the case that we are sure about the fistula type, if we know preoperative Doppler findings and dialysis treatment problems, we can determine the exact fistula site and type of complication by color Doppler sonography. The complication can be documented by spectral signal analysis; it can be shown in numerical frequency in KHz which directly points to the blood flow. Differences in flows in KHz of each fistula component, and a comparison of their interferences enable quite a precise diagnosis of stenosis and its localisation on fistula. These assumptions are based on the fact that an ideal fistula should have equal blood flow in all three components (arterial limb–anastomosis–venous limb) which is shown in KHz frequency. The

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mutual relation between these components in normal fistula should be 1; all significant standoffs point out stenotic changes and can be graphically presented, as it is seen in our examinations (Fig. 1, 2). Color Doppler sonography is an adequate examination for imaging AV fistula complications, but angiography seems to be more accurate. Middleton (5) emphasises that a digital subtraction angiography has to be the initial examination for all AV fistula complications. We agree with this opinion, especially when AV fistula complication is planned to be treated by percutaneous transluminal angioplasty (PTA).

Materials and methods – From October 1986 to October 1990, 26 patients with AV fistula were examined by color Doppler sonography and angiography. The combination of both examinations confirmed the following (Table 1): 31

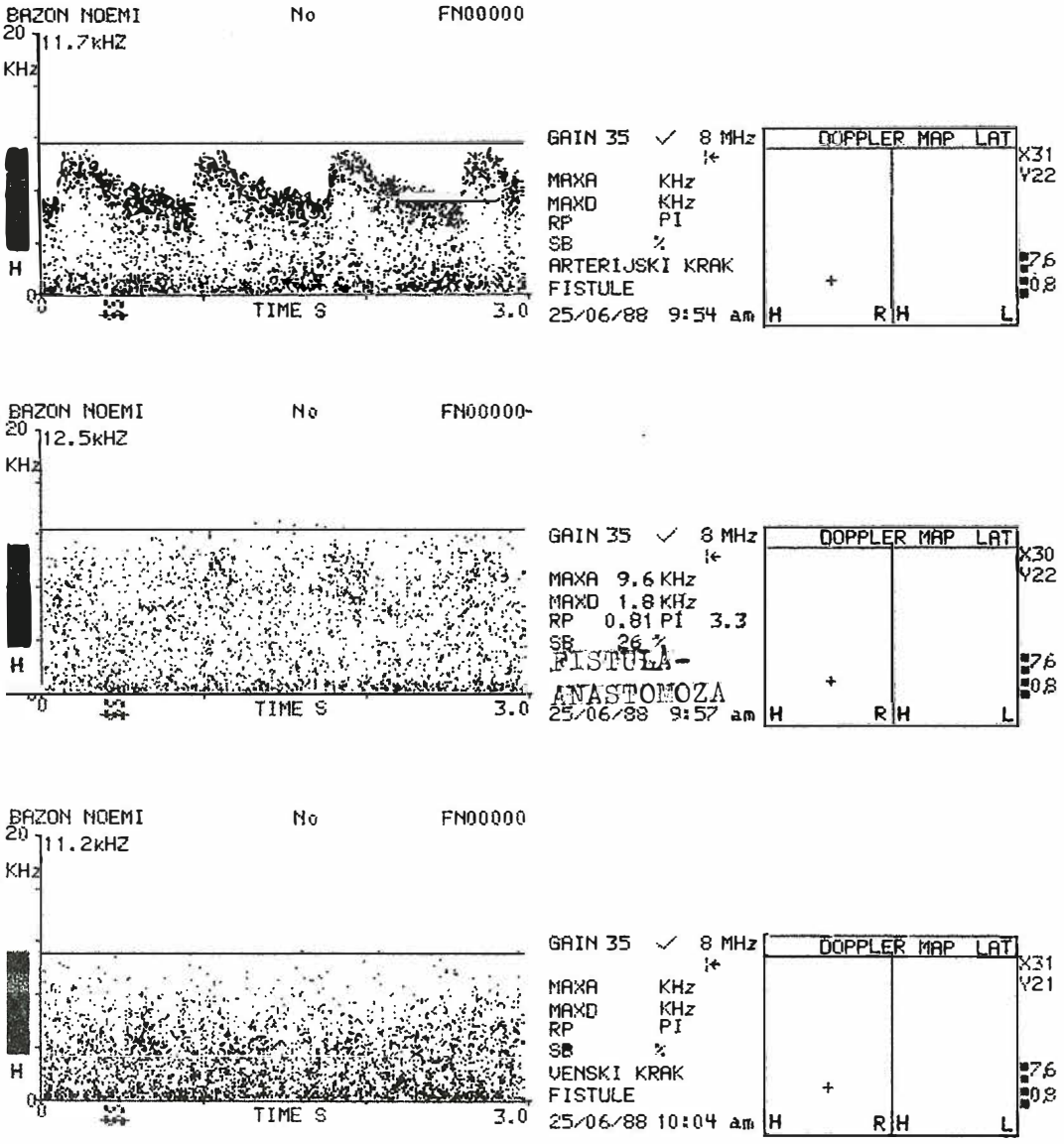


Fig. 1 – Doppler of AV fistula (normal finding)

complications in 26 patients; 10 AV fistula complications were treated by PTA. Angiography was performed by brachial artery puncture. Following Seldinger's method, a catheter of 5 FR was introduced into the artery over a metal wire conductor and 20 ml of diluted contrast medium (Omnipaque) was injected into it. The contrast flow was diascopically imaged on a TV monitor; we recorded the radial artery, anastomosis and cephalic vein (Fig. 1). Using venous puncture, we performed venography with 20 ml of diluted Omnipaque. Before the injection, the upper arm venous flow was stopped by a pressure cuff. After contrast injection, the vein, anastomosis and artery were shown and the cuff was released. All angiographically confirmed stenoses were also treated by PTA. A straight soft top wire–guide (Terumo) was positioned into the

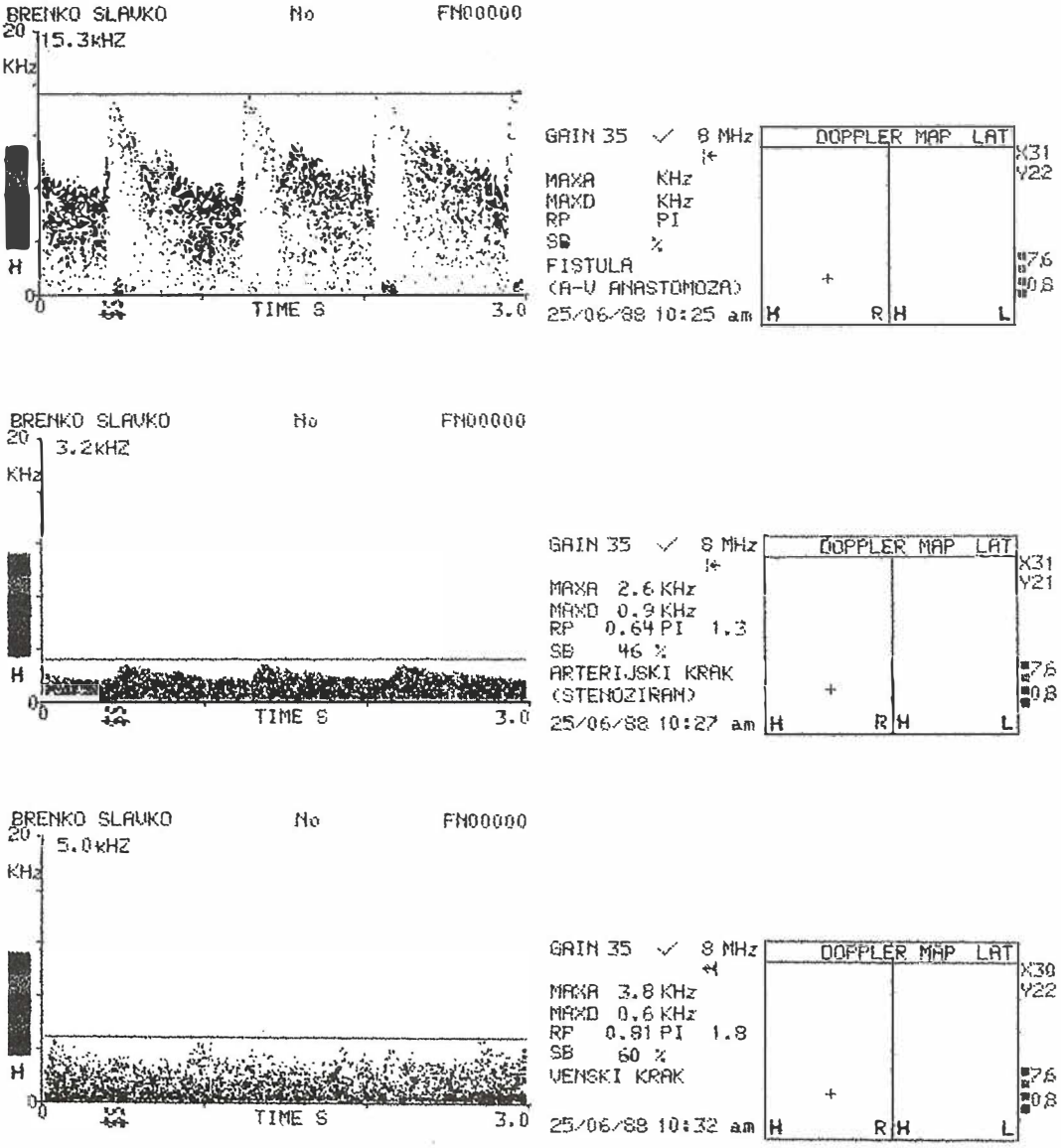


Fig. 2 – Doppler of AV fistula (stenotic arterial limb)

Table 1 – AV fistula complications: results of Doppler sonographic and angiographic examination

Complication	No	Treatment
Thrombosis	13	Surgical
Multiple venous stenoses or longer than 8 cm	8	Surgical
Radial artery stenoses	3	PTA
AV anastomotic stenoses	2	PTA
Venous stenoses shorter than 4 cm	5	PTA
Total	31	

stenosis, then a dilatation balloon catheter was introduced into the stenotic site. Prior to the balloon inflation, 5.000 units of heparin were injected through the cateter. 1% of xylocain was infiltrated around the stenotic site. Balloon catheter was kept inflated for 1-2 min. and the treatment was repeated several times. After dilatation, the balloon catheter was removed trough the wire–guide (Fig. 3, 4, 5).

Results – In 10 fistulas treated with PTA, we have obtained the following results: after the

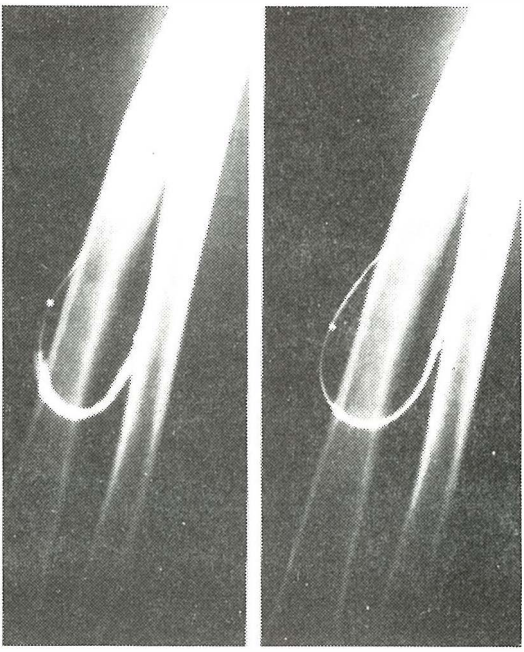
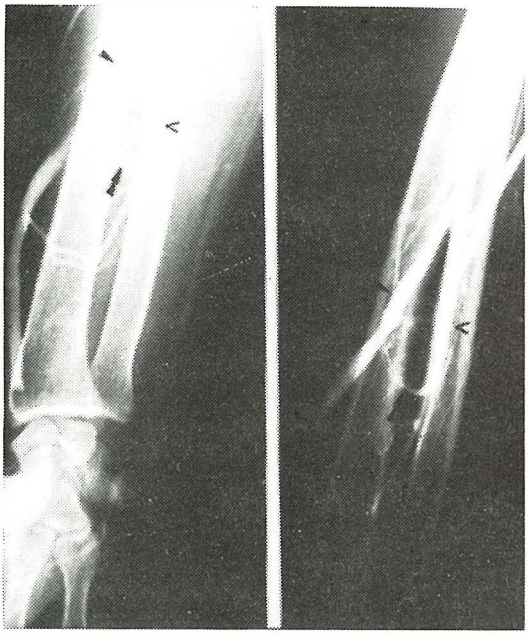
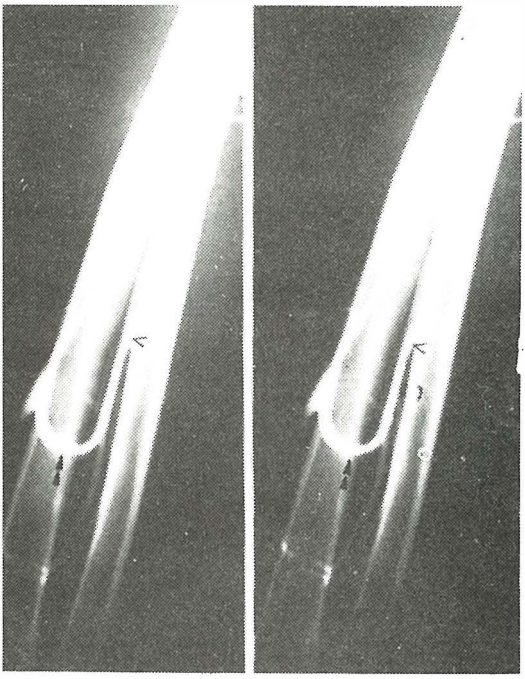


Fig. 4 – Balloon catheter in stenotic fistula site



Legend: black arrow – arteria radialis
closed black arrow – vena cephalica
double black arrow – anastomosis of AV fistula

Fig. 3 – Forearm angiogram



Legend: double black arrow – dilatated venous limb
open black arrow – arteria radialis

Fig. 5 – Forearm angiogram after PTA dilatition of the stenosis

initial success, one radial artery stenosis and one venous stenosis failed two weeks after the treatment due to a thrombosis. AV fistula anastomosis ceased to function 4 month after PTA dilatation. Successful PTA results were achieved in 4 venous stenoses shorter than 4 cm, in 2 radial artery stenoses and in one anastomosis (Fig. 6, 7, 8, 9). We achieved good result in 7 cases (70%) and the treatment was unsuccessful in 3 cases (30%).

Discussion – The first percutaneous transluminal angioplasty was done in 1964 by Dotter and Judkins in a woman who had a popliteal

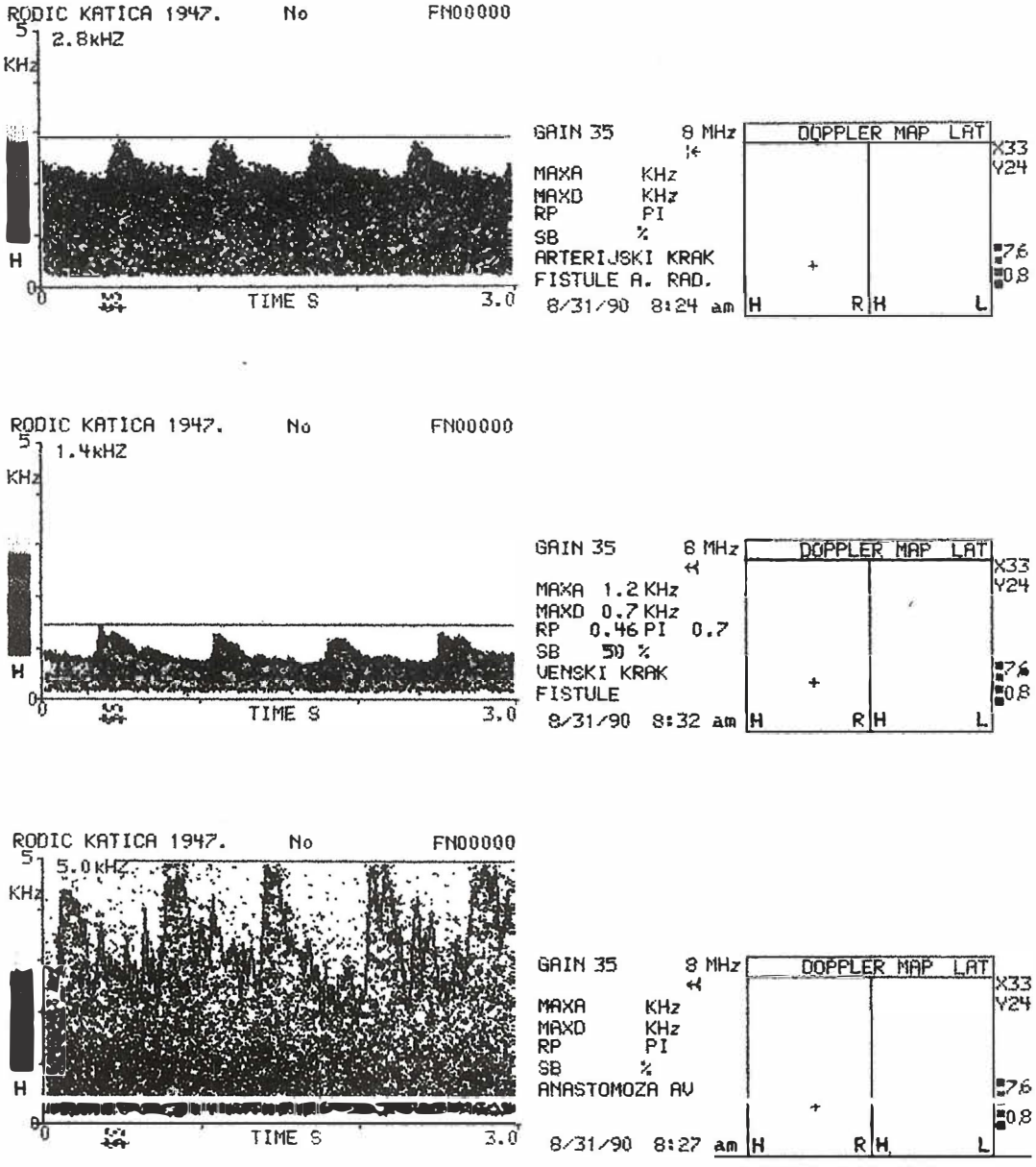


Fig. 6 – Frequency record in venous limb is different than in arterial one and in anastomosis of AV fistula. Difference is demonstrated graphically.

arterial stenosis. PTA became generally accepted treatment method in 1974 when Gruntzig developed a double–lumen balloon catheter (6). It is used as a conservative and standard method in the treatment of numerous blood vessel stenoses, such as popliteal, iliac, renal and coronary artery and, nowadays, in arteriovenous fistula complications. Hunter et al. reported 31 patients with 45 failing episodes and AV fistula dilatations (7), Glantz et al. 56 dilatations by PTA in 51 patients (8), Katzen et al. 70 dilatations (9). Similar series are noted by Martin et al. (10), and Novelline (11). The results are suggestive of further method improvement and more frequent usage. Stenoses of AV fistula components represent the most frequent dysfun-

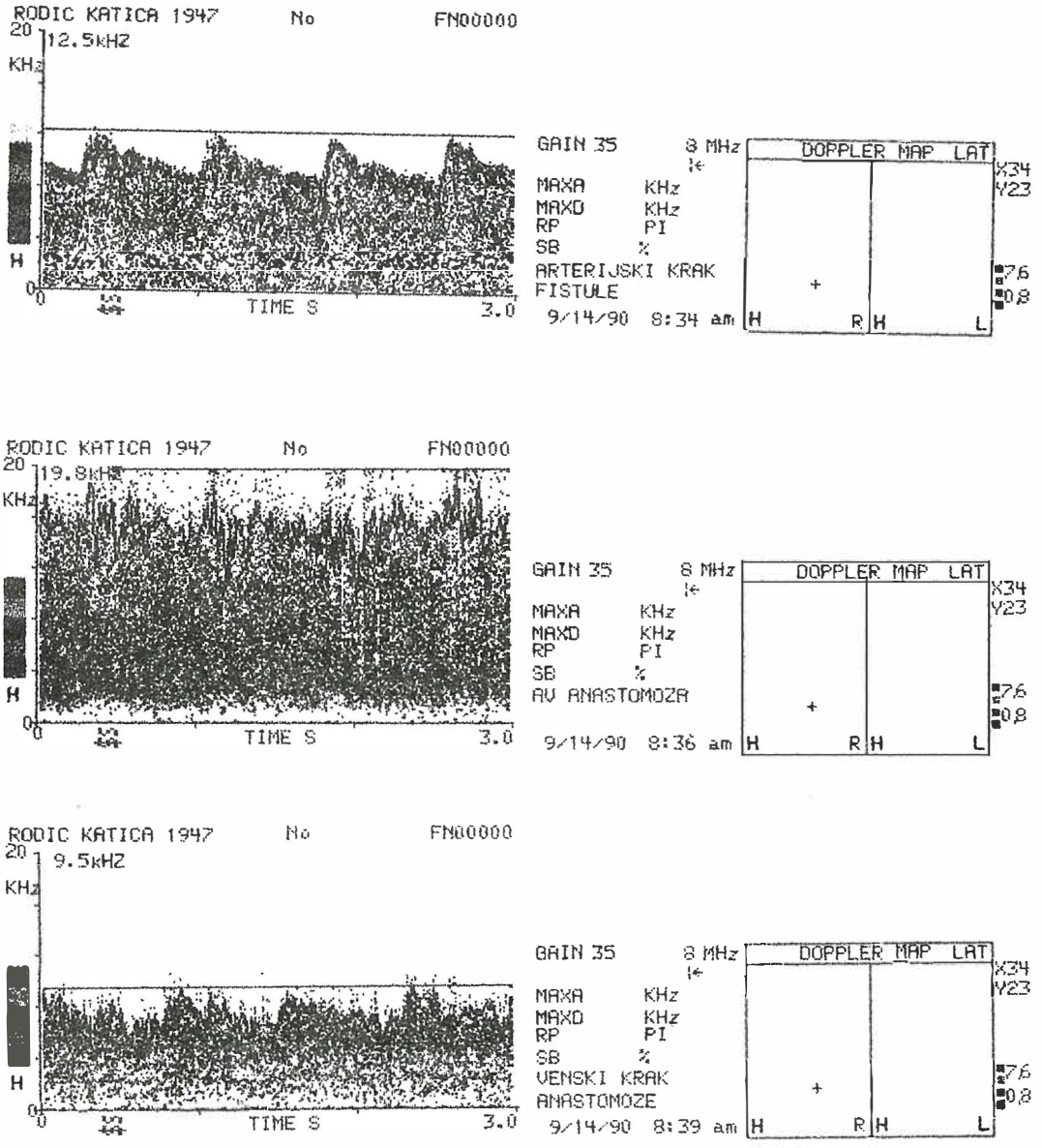
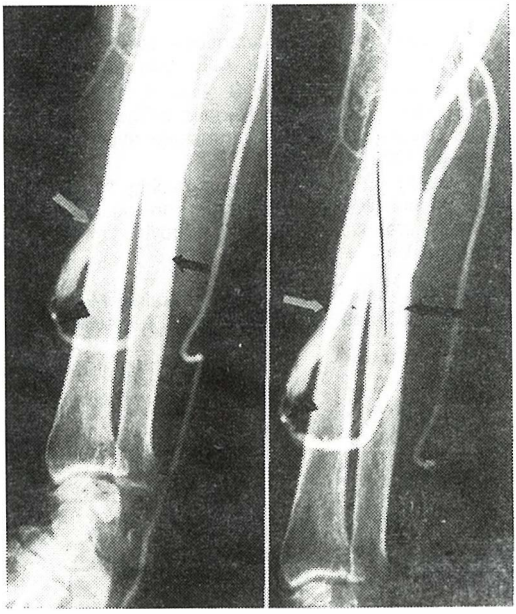


Fig. 7 – Frequency record almost identical in all three fistula limbs. Value in KHz 1 in all three fistula limb presentations

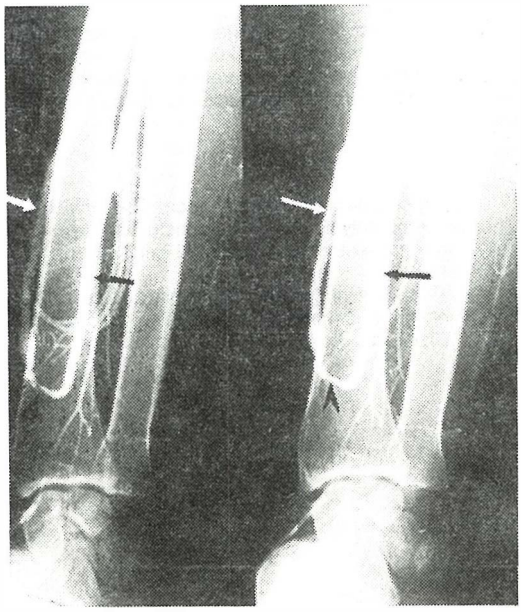
ction, and from the therapeutic point of view, the most severe late complications (12, 13). If certain norms are respected, PTA is the most effective of stenotic treatments. Our best results are associated with these criteria. Exact anamnesis during dialysis, together with color Doppler sonography and angiography give a proper diagnosis of the type of complication and its localisation. A precise image of the fistula anatomy (anastomotic type and site), as a diagnostic contribution, enables the choice of proper moment when to perform PTA, or whether a conservative treatment is needed at all. All venous stenoses longer than 4 cm, although successfully recanalizated, are mostly unsuitable for PTA treatment and require surgical correction (8, 12). Neither is PTA successful in fistulas that have failed after construction, nor in those occlusions caused by acute thrombosis (12). It is very difficult to treat venous stenoses because of their severe fibrosis, therefore, frequent long and repeated balloon catheter dilatations are necessary; the catheter radius is wider (6 to 8 mm) than blood vessel radius (7, 12), with pressure of 8 to 10 atm. The evaluation criterium for successful PTA is dialysis of the same fistula for at least 6 months, with an adequate flow rate. PTA is a method of choice in the treatment of venous stenoses shorter than 4 cm. Its advantage is a low price, noninvasive treatment which can be repeated, hospitalisation is not necessary, further surgical correction of the complication is always possible. If we have in mind only a few adequate sites for AV fistula construction and how long its functional duration should be, in spite of numerous punctures (3 times a week for years), it could be undoubtedly concluded that PTA contributes to the patient's benefit and replaces frequent surgical fistula interventions. An acute inner bleeding is the only contraindication for PTA.

Conclusion – Percutaneous transluminal angioplasty of a stenotic fistula, which is used in the regular hemodialysis, is a very simple and safe procedure, practically without complications. It is a method of choice in the treatment of stenotic fistulas. The method is much quicker, simpler, cheaper, less painful than surgical therapy and can be repeated. A failure of PTA does not exclude the possibility of further surgical correction.



Legend: black arrow – radial artery
short black arrow – the site of occlusion

Fig. 8 – Angiography of terminoterminal arteriovenous fistula of the forearm.
Occlusion of the fistula



Legend: black arrow – radial artery
white arrow – cephalia vein
open black arrow – the site of dilated arteriovenous limb.

Fig. 9 – Arteriography of terminoterminal arteriovenous fistula of the forearm
Angiogram after PTA

Sažetak

PERKUTANA TRANSLUMINALNA ANGIOPLASTIKA: TERAPEUTSKI POSTUPAK KOMPLIKACIJA ARTERIOVENSKE FISTULE ZA HEMODIJALIZU

Od listopada 1986 do listopada 1990 u Centru za hemodijalizu Pula tretirano je perkutanom transluminalom angioplastikom 10 komplikacija arteriovenskih fistula u bolesnika na redovnoj hemodijalizi. Do 1986. u dijagnostici komplikacija, osim fizikalnih metoda, korištene su invazivne pretrage: arteriografija i venografija. Od 1986. u dijagnostičke svrhe redovno se koristi neinvazivna metoda Doppler sonografija. Kada se predviđa PTA, s Doppler sonografijom se kombinira angiografija. U navedenom periodu je Doppler sonografija i angiografija korištena 31 put u 26 bolesnika. Tim je postupkom utvrđeno: 13 tromboza AV fistule, 8 stenoza venskog kraka dužih od 8 cm ili se radilo o multiplim stenozama. U 3 slučaja utvrđena je stenoza proksimalnog kraka arterije radijalis, u 2 stenoza anastomoze, u 5 stenoza venskog kraka fistule kraća od 4 cm. Opisana je tehnika dilatacije stenoza s PTA balon–kateterom. Zbog velike otpornosti stenoza na dilataciju (jaka fibroza), za dilataciju su korišteni polivinil balon kateteri s tlakom od 8 do 12 atm. Inflacija balona kod dilatacije trajala je do 2 minute a ponavljana je i do 10 puta. Za kriterij uspjeha PTA uzeto je trajanje dijalize najmanje 6 mjeseci od terapije na istu fistulu uz adekvatni protok. Od 10 fistula tretiranih s PTA 1 arterijska i 1 venska stenoza zatajile su 2, odnosno 4 tjedna od postupka, a stenoza anastomoze nakon 4 mjeseca. Kod 4 venske, 2 arterijske i 1 stenoze anastomoze tretman je bio uspješan po navedenim kriterijima. I prema našem iskustvu PTA je terapijski postupak izbora kod stenoza venskog kraka ne dužih od 4 cm, dok druge komplikacije zahtijevaju kiruršku korekciju.

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DUPLICATION OF THE COLON AND ILEUM, HEMIVERTEBRA, MALFORMATION – A RARE COMBINATION OF ANOMALIES

Frković M, Mandić A, Bradić I, Zupančić B

Abstract – The authors have presented a case of a 4-month old infant with spherical duplication of the colon (i. e. of the cecum, ascending, transverse and descending colon), and tubular duplication of the ileum, associated with the anomalies of rotation and fixation of the bowel of nonrotational type, as well as hemivertebra of the 12th thoracic segment. The preoperative diagnosis was primarily based upon the data obtained by double contrast examination of the gastrointestinal tract. The diagnosis was surgically and histologically confirmed.

UDC: 616.348-007.256:616.711-077.2

Key words: abnormalities, multiple, colon-abnormalities, spine-abnormalities

Case report

Radiol Iugosl 1991; 25:193-6.

Introduction – Bowel duplications are congenital, relatively rare anomalies. Usually, they are segmental. Their shape can be spherical or tubular, depending on whether or not they communicate with the real bowel lumen. They can occur at all levels of the alimentary tract. The wall structure of the duplication cysts can imitate bowel wall structure of any intestinal segment. Duplications are often associated with other congenital anomalies, i. e. genito-urinary and vertebral. In 1884 Reginald Fitz published first description of a colonic duplication. The term »duplication of alimentary tract« which is used now was given by Ladd in 1937 (1).

The most common location of duplications is the ileum (2, 3, 4). Colonic duplications are less common, and until today only 50 cases have been reported (3, 5). Duplications can be multiple in 15% of cases (1). Vertebral anomalies occur in 15% (1).

The authors present a 4-month old infant with a spherical duplications of the colon from the cecum to the sigmoid, and tubular duplication of the ileum, associated with a nonrotational anomaly of rotation and fixation of the bowel, associated with hemivertebra of the 12th thoracic segment.

Case Report – A 4-month old infant was admitted to the Pediatric Department because of suspected abdominal mass. He also had right inguinal hernia.

During the first months of life, the child who was delivered spontaneously, on term, from the third pregnancy after two miscarriages, grew well. From the time of birth the mother noticed an abnormal curvature of the spine. On routine check up the abdomen was prominent and an intraabdominal tumor was suspected. The child was referred to the Pediatric Department. On physical examination the abdomen was above the chest. An elastic mobile mass was palpated in the mid left abdomen. The child was otherwise healthy. Laboratory tests were normal. The rentgenographic examination of the thoracic spine showed hemivertebra of the 12th thoracic segment with scoliosis to the left. Ultrasound examination of the abdomen was done. Large amount of gas in the bowel made examination very difficult. Parenchymal organs were normal. No pathologic structure was found. On intravenous urography the right kidney was lower and more medially placed because of the deformity of the

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spine. The bladder was normal. Computed tomography (CT) of the abdomen showed multiple large and small masses, consisting of fat, soft tissue, and some air, located in the mid abdomen. Differential diagnostic possibilities of these CT findings were multiple abscesses, and teratosarcoma. Contrast barium enema showed almost the entire colon in the left abdominal cavity with its loops pushed ventrally and aside by an extrinsic mass. The cecum was horizontally placed and bent, with atypically placed valvula of bauchini. The appendix did not show. A segment of the ileum, shown by reflux of barium was within the right inguinal hernia (Fig. 1). The barium examination of the upper gastrointestinal tract showed horizontally, subdiaphragmatically positioned stomach. The duodenum continued in the jejunum in the right upper abdominal cavity without forming a duodenojejunal flexure. The loops of the ileum were in the right lower abdominal cavity (Fig. 2) The final diagnostic conclusion after contrast examination of gastrointestinal tract and CT of the abdomen was malrotation (nonrotational) with an extraluminal intraperitoneal mesocolic mass, and right inguinal hernia without bowel obstruction.

According to the clinical status and laboratory tests, we excluded the possibility of multiple abscesses, and listed as differential diagnostic possibilities a mesocolic chylous cyst, and spherical duplication of the colon without communication with the bowel lumen.

At surgery spherical colonic duplication was found. Proximal blind end of the duplication was dragged retroperitoneally to the right psoas muscle and attached with adhesions to the lower pole of the right kidney. Distally, the duplication extended to the junction of the descending and sigmoid colon (Fig. 3 and 4). Along the mesenteric contour of the ileum, 20 cm proximal to the valve of Bauchini, a 12 cm long duplication of the ileum was also found (Fig. 5) Schematic description (Fig. 6).

The proximal 20 cm long segment of the colonic duplication was resected. It was filled

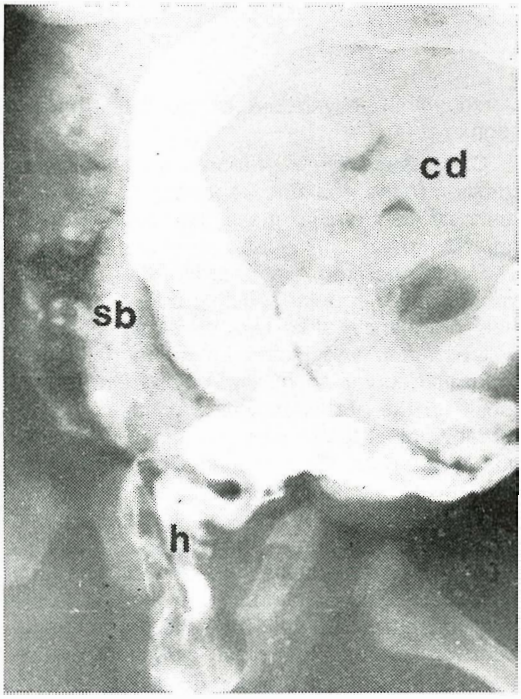


Fig. 1 – Barium enema examination – the colon is widely displaced and its mesocolic contour is slightly compressed by a huge space occupying mass (cd). The small bowel (sb) is on the right, ileal loops are in the inguinal hernia (h)

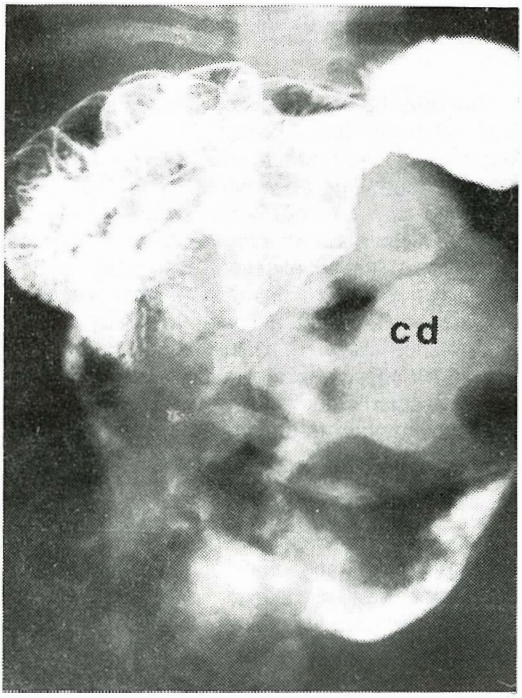
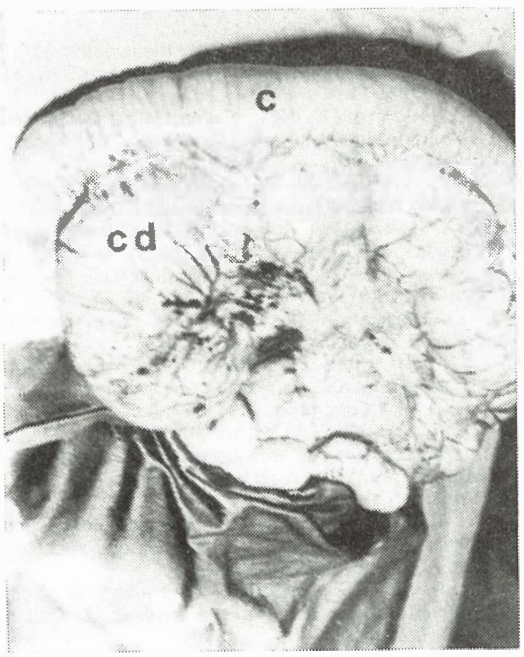


Fig. 2 – Contrast examination of the upper gastrointestinal tract – the stomach is displaced upwards, duodenum and jejunal loops are in the upper right hemiabdomen. The expansive mass (cd) is central and to the left. Barium remnant is in the rectosigmoid.



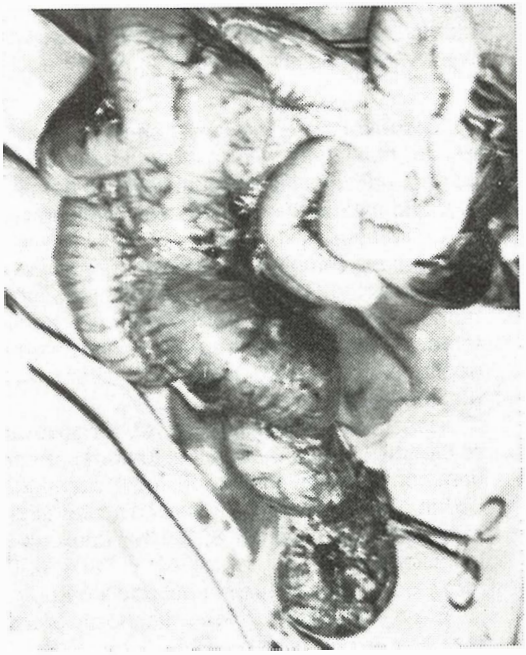


Fig. 3 and 4 – Operative finding: a spherical duplication (c – colon, cd – colonic duplication)

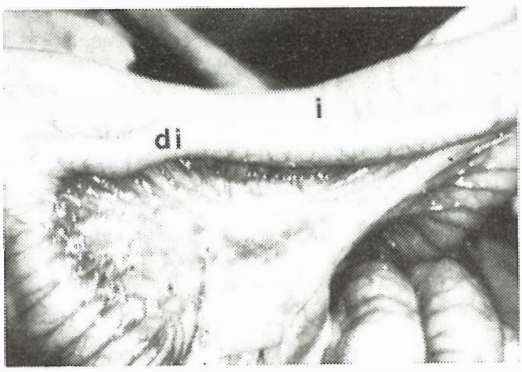


Fig. 5 – Duplication of the ileum. Operative finding (i – ileum, di – duplication)

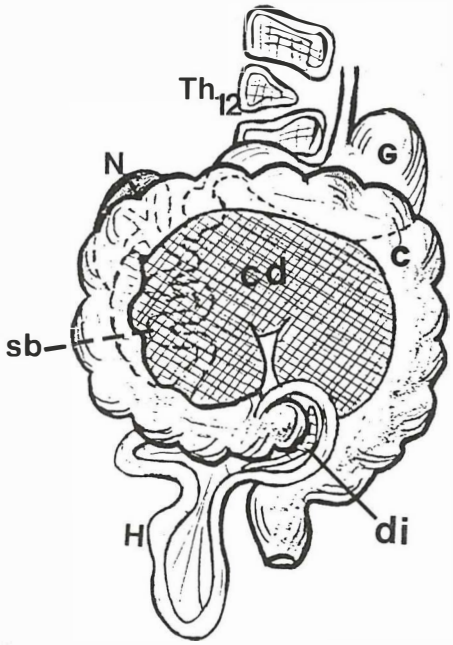


Fig. 6 – A schematic presentation: spherical duplication of the colon (cd) and ileum (di), malrotation, hemivertebra Th 12 (N – kidney, G – stomach, sb – small bowel, H – hernia inguinalis, c – colon).

with dense, pale and yellow liquid content. The distal end of the duplication was brought out as a cutaneous stoma in the left upper hemiabdomen. The histologic examination (No. 3970/90) showed that the wall of the duplication had the same structure as the wall of the colon.

Two months later, the baby had a second operation. A side to side anastomosis of the remaining colonic duplication segment with distal

part of the colon was made and the cutaneous stoma closed. Both postoperative recoveries were without significant complications.

Discussion – The case report presents a 4 month old infant with a voluminous spherical colonic and tubular ileal duplication, hemivertebra, and malrotation of the bowel. Until now, only a small number of cases of multiple colonic duplications combined with other anomalies have been reported (1). Three of these cases presented colonic duplication associated with hemivertebra. All three cases were also associated with genitourinary tract anomalies (1). There was no genitourinary anomaly in our case.

Because of complications, as an obstruction of the bowel, or an abdominal tumor as the most common, duplications are in most cases identified in the first months of life. This was also the case with our child. In 85%, the duplication is identified before the age of two (1, 2, 5, 6, 7). It rarely passes undetected until adulthood (8).

Even with modern, highly diagnostic procedures, the exact preoperative diagnosis of this anomaly is rare (9). Because of malrotation the possibility of mesocolic chylous cyst was raised. In malrotation they usually appear due to disturbance in the lymphatic drainage, caused by chronic volvulus (10, 11, 12, 13). The presence of hemivertebra reminded us of similar cases in literature, i. e. the combination of hemivertebra with colonic duplication (1).

The therapy for duplication is surgical. The type and the extension of an operation depends on the location, volume, vascularity, and preoperative complications, caused by duplication.

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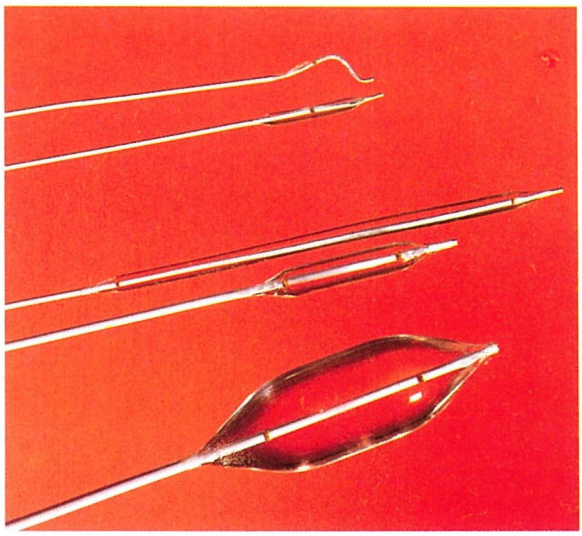

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CLINIC FOR LUNG DISEASES »PODHRASTOVI«, SARAJEVO

TRACHEOBRONCHOMEGALY (MOUNIER–KUHN SYNDROME)

Dalagija F. Dizdarević Z. Bešlić Š. Đurković P

Abstract – Tracheobronchomegaly (Mounier–Kuhn syndrome) is a very rare, probably congenital, disorder. Its clinical appearance, in the form of chronic inflammation symptoms of the respiratory tract, is non-specific. Radiological features are, however, unequivocal, thus leading to the correct diagnosis. But, such patients can remain undetected if they are asymptomatic or if only conventional radiography is used. Since the detection of this anomaly by CT is simple and accurate, it is suggested in all patients with recurrent infections of the respiratory tract. This report presents a 55-year-old patient with this rare condition.

UDC: 616.23-007.61

Key words: tracheobronchomegaly

Case report

Radiol Iugosl 1991; 25:197-200.

Introduction – Tracheobronchomegaly (TBM) is defined as a marked dilatation of the trachea and main bronchi. The first description of its pathologic changes is credited to Czylharz in 1897, but it was not until 1932 that the first clinical description was published by Mounier–Kuhn (1, 2, 3, 4, 5).

The clinical presentation is non–specific. There are symptoms, frequently since the early childhood, of chronic respiratory tract disease, i. e., loud cough with or without sputum production, recurring pneumonia, hoarseness and even spontaneous pneumothoraces. Radiological features are, however, unequivocal, thus leading to the correct diagnosis. They are: marked dilatation of the trachea and main bronchi, tracheal diverticulosis, bronchiectasis and chronic inflammatory changes of the lung parenchyma (1, 2, 5, 6).

TBM is a very rare disorder and only 82 cases were reported in the literature since 1988. However, some patients with tracheobronchomegaly may be totally asymptomatic and are not detected, whereas those with symptoms frequently are overlooked if chest radiography alone is used for diagnosis (4).

The detection of TBM by CT is simple (and straightforward). It is believed that with wide application of CT in patients with recurrent pulmonary infections, more cases of tracheobronchomegaly can be identified in the future (4, 7).

Case report – A 55-year-old mailman, cigarette smoker of long duration with the recurrent pneumonia right, chronic rhinopharyngitis and maxillary sinusitis, was reffered to the Clinic of lung diseases for investigation and treatment.

The pulmonary function tests revealed an increased resistance in respiratory tubes, causing an moderately severe ventilatory insufficiency of the obstructive type, followed by the averagely marked hyperinflation of lung parenchyma.

Chest radiograph showed the increased markings in both peribronchovascular lobes, especially on the right side basally, with stained–honeycomb shadows. Bronchograpy was performed because of the suspected right bronchiectasis. The finding was impressive: a marked dilatation of the trachea and both main bronchi with ring–like enlargement, as the intestinal haustrum. Diascopy demonstrated a marked narrowing of the lumen during expiration, and contrast medium did not pass into the far periphery.

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Right bronchial tree had »scattered« bronchiestases. The presence of TBM with diffuse bronchiestases on the right side was concluded (Fig. 1).

During rehospitalisation, CT of the thoracic organs was performed. Transversal CT slices showed a greatly dilated trachea with a diameter of 4 cm, square in places, with sharp irregular contures (Fig 2). Both main bronchi were dilated with a diameter of 2,5 cm right and 2,4 cm left (Fig. 3). Para and retro–cardiobasally, lung markings were expressive, rough, partially irregular, with post–inflammatory and deformative changes (Fig 4).

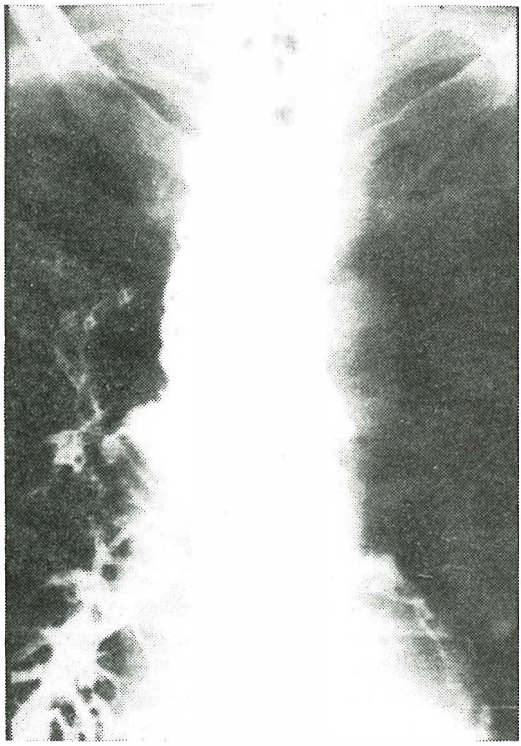

Fig. 1 – PA bronchogram: marked dilatation of trachea and main bronchus with bronchiectasie right.

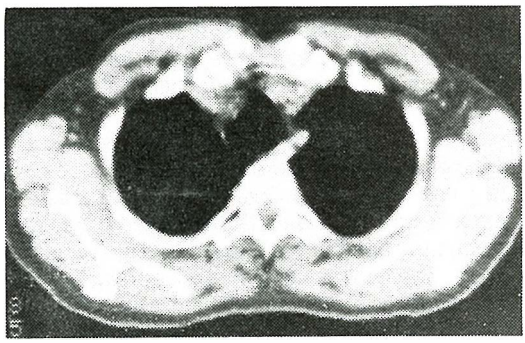

Fig. 2. – CT slice: marked dilatation and deformity of trachea.

Discussion – Tracheobronchomegaly (TBM) has been described by a variaty of names, including tracheobronchiectasis, tracheal diverticulosis, tracheocele, tracheomalacia, tracheobronchopathia malacia, and any diameter of the trachea that exceeds 3 cm (1), over 22 mm in men and 19 mm in women (8) is diagnostic for TBM, as well as the diameter of the right main bronchus over 2,4 cm (1), over 16 mm (8) and

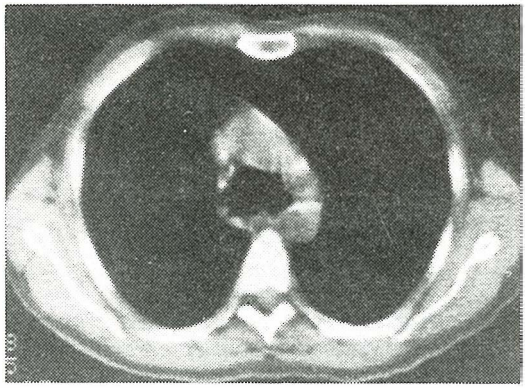

Fig. 3 – CT slice: marked dilatation of trachea and both main bronchi.

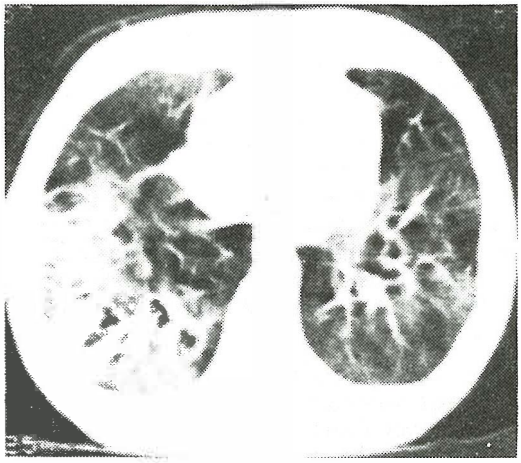

Fig. 4 – CT slice: postinflammatory and deformative changes retrocardiobasally right.

left main bronchus over 2,3 cm (1) over 14 mm (8).

The cause of TBM is unknown, although most authors believe in the congenital etiology. The first comprehensive description of the pathologic changes in TBM is credited to Czyhlarz who in 1897 noted »marked atrophy of the longitudinal elastic fibers and thinning of the muscularis« in a postmortem specimen, suggesting a congenital weakness of the walls«. Although the association of this condition with Ehlers–Danlos syndrome reported in adults and with acquired cutis laxa in children (9) may suggest a congenital defect in connective tissue as the basis for TBM, most cases, however, presented in the third or later decades of life and showed no evidence of other connective tissue disorders (4), as do other congenital lesions such as polycystic kidney (7).

According to some authors, TBM is believed to be an acquired rather than a developmental anomaly (2, 10, 11). It has been speculated that barotrauma is the primary pathopysiologic factor in neonates who have TBM after receiving intensive ventilatory and oxygen support, as well as the inhalation of chronic irritants found in cigarette smoke and air pollution, in adults (2, 12). But it seems likely that smoking and other irritants exacerbate the condition rather than cause it (7).

There is an almost invariable history of chronic infection, but this could just as easily be a result as the cause of the widened airways. A number of authors note the existence of TBM without clinical and pathologic evidence of inflammation and point out that while chronic inflammatory lung disease is common, TBM is rare. This further militates against TBM being an acquired disorder (1, 5, 7, 13). The consensus seems to be that there is a congenital anomaly, with or without overlying inflammatory changes (1, 5, 13, 14).

Our patient is a cigarette smoker of long duration and besides the chronic rhinopharyngitis and maxillary sinusitis, this presents one of the causes of recurrent pneumonia.

Radiographically, TBM is manifested by the marked dilatation of trachea and main bronchi with irregularly corrugated conture of the air columns, considered as a consequence of the protrusion of redundant musculomembronous tissue between the cartilaginous rings (4). The severe pass on the normal caliber of the termal airways has been presented as the bronchographic characteristic of TBM (3.). Grossly enlarged but weakened airways and insufficient cough mechanism impede mucociliary clearance and lead to retention of mucus with resultant recurrent pneumonia, emphysema, bronchiectasis and parenchyma scarring (4, 5).

CT, with the transversal slices, is superior over the standard radiography and conventional tomography because of the possibilities of accurate measurements of the tracheal and bronchial dilatation, and early and precise diagnosis of parenchymal changes and calcification. An expiratory collapse of the trachea and the main bronchi can also be identified by CT, but can normally be easily visualized by fluoroscopy. Discrete changes of the bronchial walls, like small diverticula, are best shown by bronchography (6, 7, 15, 16, 17).

Although only 82 cases of TBM have been reported, the actual number of cases could be much higher. Most cases of TBM probably are underdiagnosed if they are asymptomatic and if chest radiographs alone are used (the present case is such an example). Such patients are treated as the cases of chronic bronchitis or repeated pneumonia, not taking into account this anomaly (3, 4). Because TBM can be easily overlooked on plain chest film, and its detection by CT is simple and straight forward, CT should be done in patients with chronic recurrent pneumonitis for the detection and evaluation of underlying predisposing conditions, including TBM (4).

Conclusion – Although the diagnosis of TBM in our patient was made by a previously performed bronchography, this anomaly, – syndrome – could be easily and accurately detected by CT. This is evident from the presented CT scans, and is in accordance with the reports in literature. Therefore, we support the suggestion that should be used patients with that CT should be used in reccurent pulmonary infections.

Sažetak

TRAHEOBRONHOMEGALIJA (Sindrom MOUNEIR–KUHN)

Traheobronhomegalija (Sindrom Mounier–Kuhn) predstavlja izrazito rijetku, vjerovatno kongenitalnu, anomaliju. Njene kliničke manifestacije, u vidu simptoma hroničnih upala respiratornog trakta, su nespecifične. Radiološki znaci su karakteristični i vode do tačne dijagnoze. Međutim, ovi pacijenti mogu ostati neotkriveni, ako su bez simptoma ili ako se koristi samo standardna radiografija. Pošto je detekcija ove anomalije, pomoću CT, jednostavna i pouzdana, to se on preporučuje kod svih pacijenata sa hroničnim recidivirajućim upalama respiratornog trakta.

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ULTRASONOGRAPHICALLY GUIDED PERCUTANEOUS THERAPY OF LOBAR NEPHRONIA

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Abstract – In our patient the diagnosis of lobar nephronia (acute focal bacterial nephritis) was suspected on the basis of anamnesis, status, laboratory data and ultrasonography. A cytological examination of the specimen confirmed the diagnosis. Four times repeated instillation of Gentamycin (80 mg) »in loco« under ultrasound control resulted in the complete regression of local lesion.

UDC: 616.61-002-073:534-8

Key words: nephritis-therapy; ultrasonic therapy

Case report

Radiol Iugosl 1991; 25:201-4.

Introduction – Lobar nephronia (acute focal bacterial nephritis) is a clinical entity which can be defined as an acute local infection of renal parenchyma without liquefaction (1, 2). In 90% of cases the infection was caused by e. coli and rarely by aerobacter aerogenes, pseudomonas aeruginosa, proteus and klebsiella (3, 4). Clinical symptoms correspond to acute pyelonephritis.

Regarding ultrasonical examination the following possibilities should considered in the differential diagnosis: mixed tumor, column of Bertini, hematoma, lymphoma, urinoma and cyst (1, 5, 6). Some specific characteristics of focal lesions such as poorly limited solid mass usually with low-level echoes which disrupt continuity of the corticomedullary border (1, 2) and physician's experience improve the diagnosis.

Ultrasonically guided punction and cytological examination of the specimen are the methods of choice for final diagnosis (1, 4, 5, 7). Local topic antibiotic application (1, 5, 7) or ultrasonically controlled percutaneous drainage (1, 5, 7, 8) proved to be successful therapeutic procedures.

Case Report – A 58-year old man was referred to the Department of Nephrology (152/90) as an emergency case after an episode of left flank pain, high temperature and dysuria during the last four days. He said that he had urinated blood several times. In the remaining history, he underwent malaria in childhood and a few attacks of erysipelas on the shin, joint inflammation and inflammation of the urinary system with symptoms which were similar with the present ones and passed spontaneously. Physical examination revealed positive left lumbar succussion and palpation tenderness of the lower half of left kidney area.

Laboratory data: urine lucid, yellow, sour, alb+ (4.3 g/1), sugar+ (1.6 mmol/1), acetone+. Microscopic specimen of urine: white blood cells, bacteria, 4-6 RBC. Urinoculture: e. coli (> 100.000 per ml), Hemoculture: e. coli, SR 80/, WBC 9.8 BS 14.1, urea 10.1, creatinine 149. All other biochemical investigations were normal.

After anamnesis, status and laboratory data the working diagnosis was: urosepsis, acute left–side pyelonephritis and diabetes mellitus.

An i. v. urography showed that the left kidney inefficiently concentrated contrast with pallid nephrographic effect and incapability of pyelocaliceal system analysis. The left kidney was enlarged with irregular borders which corresponded to an expansive process and further treatment was recommended.

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Ultrasonography revealed gently hyperechoic area (2.6 x 2.3 cm) of the medial part of the left kidney which pressed echoes from the pyelocaliceal system. According to the sonographic findings, this focal lesion is probably column of Bertini. In the differential diagnosis lobar nephronia, which is often hypoechoic, has to be taken into consideration. The right kidney, liver and gallbladder were sonographically normal. The prostate showed sonographic signs of chronic prostatitis with a few prostatoliths. Ultrasonically guided percutaneous puncture of the left kidney was recommended (Fig 1).

Ultrasonically guided puncture was done in the following way: the patient lied on the right

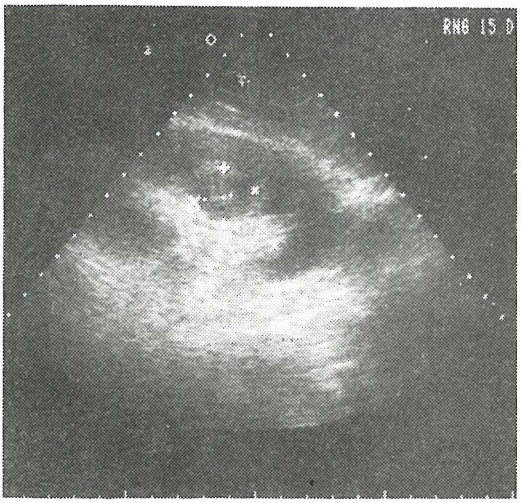

Fig. 1 – Dorsal axial sector scan of the left kidney with presentation of mesonephric focal lesion (markers)

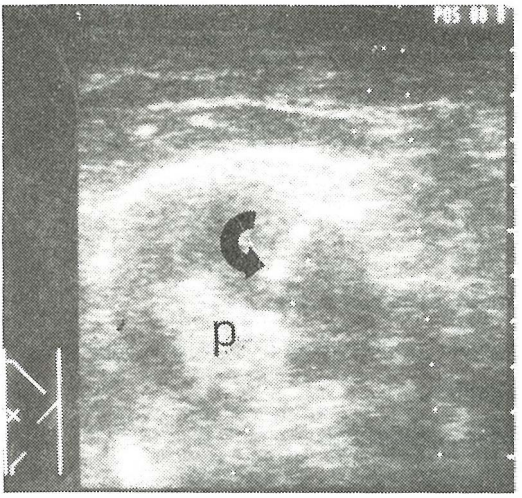

Fig. 2 – Semioblique linear feature of the left kidney during gentamycin application; hyperechogenic echoes of the pyelon (p), arrow shows the tip of the needle

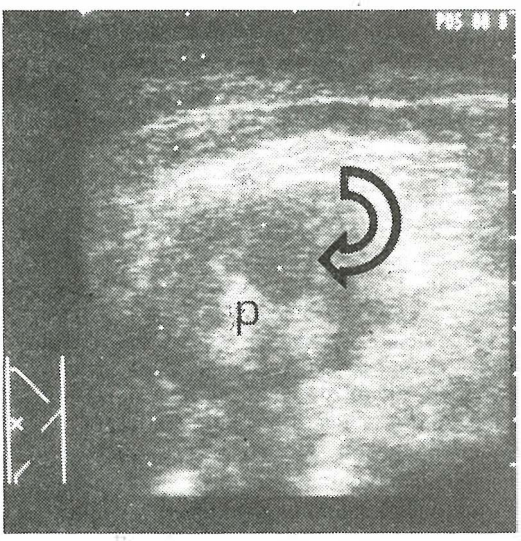

Fig. 3 – Semioblique linear scan of the left kidney after gentamycin application: hyperechogenic area caused by liquid antibiotic with microbubbles (arrow), pyelonic echoes (p)

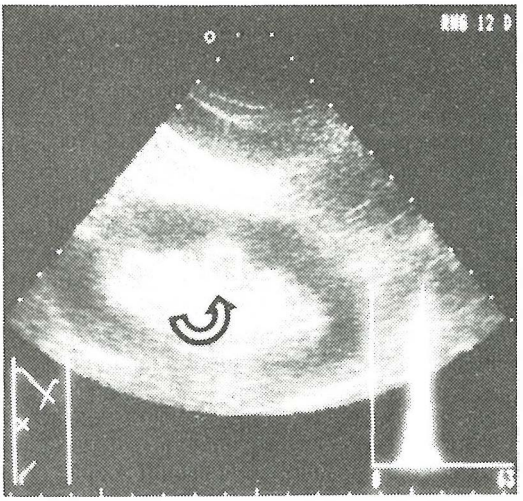

Fig. 4 – Intercostal sector scan of the left kidney after therapy; hyperechogenic area in the medial part of renal parencyma (arrow) caused by fibrosis after inflammatory process healing, with histogram

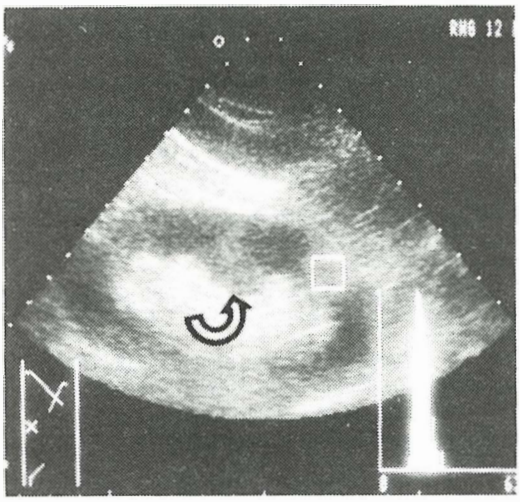

Fig. 5 – The same scan as in Fig. 4; arrow shows a clear hyperechogenic region; histogram was taken from normal surrounding renal parenchyma (note the various curves and numbers)

flank, upper part of the abdomen was bolstered for better kidney fixation. Sterilisation and confining of the operative field was done with standard solution and sterile compresses. With a sterilised ultrasound probe of 3.5 MHz the best position for puncture was fixed which meant that there was enough »protecting stratum« of healthy parenchyma between the lesion and renal capsule to prevent the possibility of bacterial propagation into the perirenal compartment. Skin incision (2-3 mm) was done under local anaesthesia. Pathological process as set in the position which corresponded to puncture-line of the probe. Following puncture–line, a thick needle was stung through the lumbar muscles. It served as a canal for a thin aspiration needle with aspiration biopsy of focal kidney lesion was performed 4-5 times under the negative pressure. Cytologic specimen was prepared in standard way.

The cytologic specimen showed dense mass of mature WBC and some macrophages.

After sonographic and cytological confirmation, a therapy was started as follows: four times, every 3-4 days, gentamycin (80 mg) was applied into the focal kidney lesion under ultrasound guidance. Application procedure was the same as described previously. Antibiotic was injected directly »in loco« with a syringe through needle along the guideline (Fig 2 and 3).

With the therapeutic procedure described, the regression of focal kidney lesion was complete and the patient was discharged with recommendations for home care. Ultrasound follow-up examination after 3 weeks did not show presence of residual disease. Hyperechogenic area and its histogram analysis corresponded to fibrosis (Fig. 4 and 5).

Discussion – It noninvasiveness, painlessness, the possibility of repetition without consequences to the patients health and accuracy of diagnosis render ultrasonography the method of choice in the detection of kidney pathology. Interventional ultrasonography, enabling visualisation of diagnostic or therapeutic procedures (biopsy, nephrostomy, punction and cyst sclerosation, application of various drugs), represents an advantage which further promotes the applicability of ultrasound. Histogram analysis of focal lesions, which is being investigated, facilitates the distinction between »pathological« and »normal«. Lobar nephronia is a localised form of pyelonephritis (2, 6, 9, 10) and is to be understood as the midpoint in a spectrum of pyelonephritis from acute pyelonephritis to abscess (6). Pathophysiologically a pronounced cortical vasoconstriction was localised in the areas of acute inflammation with clogging of the peritubular capillaries by inflammatory cells. After a few days this areas progressed to necrosis and/or abscess (10), This examination confirmed the thesis of lobar nephronia as a precursor of renal abscess.

Ultrasonography, i.v. urography and computerised tomography are the techniques used in the diagnosis of acute renal diseases. As the lobar nephronia comprises a spectrum of different pathological conditions with equal features the cytological puncture is necessary. The maturation of inflammatory process changes the sonographic image (enhancement of border echoes, separation from surrounding tissue). Liquefaction results in central hypo- or anechogeneity (1). Intravenous urography presents a solid expansive process and CT shows a wedge shape area of decreased attenuation (2). Although hypoechogenic area without increased posterior ultrasound beam enhancement is the most commonly described ultrasonographic findings in the recent literature (1, 2, 6, 9, 11), our patient had a slightly hyperechogenic solid mass, and therefore ultrasound diagnosis was implemented by sonographically guided puncture.

In the recent literature, classic parenteral antibiotic therapy is described as therapeutic procedure (2, 6, 11, 12). We decided for an intermittent topical antibiotic application with ultrasonical following of focal lesion regression.

Considering the previously mentioned advantages, complete regression was achieved after two weeks.

Conclusion – We presented a case of lobar nephronia. The disease was verified after ultrasonically guided puncture. We decided for a topical antibiotic application under ultrasonic control as a therapeutic procedure which proved to be successful. We believe that the described ultrasonically guided diagnostic and therapeutic procedures can be helpful in the treatment of some focal infections of the renal parenchyma. However, when making selection between classic therapy and that described in our report, appropriate education and experience of the physician should be of decisive importance.

Sažetak

SONOGRAFSKI VOĐENA PERKUTANA TERAPIJA LOBARNE NEFRONIJE

Prikazan je pacijent u kojeg je, na osnovu anamneze, statusa, laboratorijskih nalaza i ultrazvučnog pregleda postavljena sumnja na lobarnu nefroniju (akutni fokalni bakterijski nefritis). Izvršena je punkcija pod kontrolom ultrazvuka, te je citološki nalaz punktata potvrdio dijagnozu. U cilju terapije instiliran je u četiri navrata pod vodstvom ultrazvuka, »in loco«, Gentamicin (po 80 mg), što dovodi do potpune regresije fokalne lezije.

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A CASE OF SINCHRONOUS BILATERAL RENAL CELL CARCINOMA: ULTRASOUND, CT AND ANGIOGRAPHIC EVALUATION

Kurbel S, Filaković Z, Rubin O

Abstract – A case history of a patient with sinchronous bilateral renal cell carcinoma is presented. Diagnostic procedures are discussed briefly utlrasound, CT, and angiography proved to be complementary diagnostic modalities with their own limitations.

UDC: 616.61-006.6-073.75

Key words: kidney neoplasms–radiography; carcinoma, renal cell

Case report

Radiol Iugosl 1991; 25:205-9.

Introduction – Recently, we had a case of a patient with sinchronous bilateral renal cell carcinoma as a diagnostic problem. The ultrasound finding of bilateral but not similar massive kidney lesions has forced us to be very cautious with temporary diagnosis.

We belive that this rare case is worth presenting.

Case history – A 63 year old male patient T.J. was admitted to the Clinic of Internal Medicine, Department of Hematology, General Hospital Osijek. He suffered myocardial infarction 5 years ago. Since then he had non serious hearth troubles except moderate hypertension. Two years ago he was hospitalised in another hospital because of anemia, accelerated sedimentation rate and unexplained fever, but no serious disease was revealed at that time. He had no documentation of previous abdominal radiologic or ultrasound examinations.

The reason for admittance to the hospital was blunt subcostal pain in the right side of the abdomen lasting for three weeks. Short periods of fever were present almost every afternoon reaching up to 38.5°C. He felt weak and had slight nausea with occasional vomiting. No cardiac, respiratory or urinary symptoms were noted. Stool was normal. Weight loss was 5 kg in 3 weeks. A short treatment with peroral antibiotics did not improve his condition.

Some important laboratory values were altered: sedimentation rate (Westergreen) 80 mm/h, RBC 4.19×10^{12}/L hemoglobin 97 g/L, Fe 3.7 μmol/L, WBC 34×10^{9}/L with 23% of band neutrophils. Urine finding was normal without erythrocytes in urine sediment.

Abdominal ultrasound examination was performed using SONEL 3000, a mechanical sector ultrasound unit produced by CGR, France. Ultrasound probes of 3 and 5 MHz were used.

During the abdominal ultrasound examination no important changes were found in the liver, biliary ducts, gallbladder, pancreas and spleen. The upper lobe of the right kidney was occupied by an oval, well delineated zone measuring 7x5 cm (Fig. 1 and 2). The zone was slightly hyperechogenic when compared to the neighbouring renal tissue. Numerous small hypoechogenic spots rendered the image to appear «dirty». According to the categorisation of the renal focal lesions proposed by Weill and colleagueas (1), the lesion was classified as type III, lacking ultrasound signs of calcifications. Although the lesion was close to the liver, it clearly belonged

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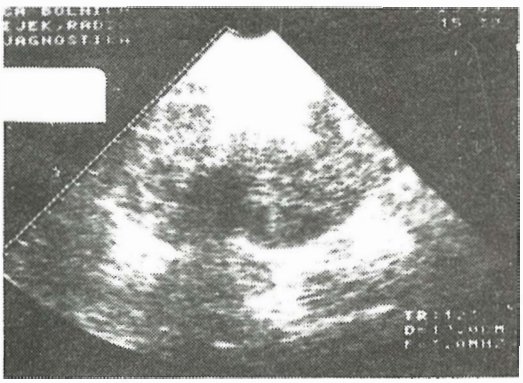
to the right kidney. The rest of the right kidney seemed normal.

The lower pole of the opposite and otherwise normal left kidney was covered with a dense hyperechogenic zone, forming a cap that contained two smooth and fully sonolucent cysts (Fig. 3 and 4). The bigger echo–free area was 3 to 4 cm in diameter. The ultrasound image of the left kidney lesion was similar to type V according to Weill, although the cystic areas were smoothly delineated and did not seem to be necrotic. This was a fully different ultrasonic image. For the difference from the lesion in the right kidney, this was a fully different ultrasonic image.

The findings of the abdominal ultrasound examination were conclusive for the presence of a large expansive process in the right kidney. Cystic lesion in the left lower lobe of the kidney was considered as a probable another tumor. Abdominal CT examination was recommended.

Computed tomography examination was performed on SIEMENS DR–H scanner at our Department of Radiology, two days later. Tumor of the right kidney was found to originate from the ventral renal cortex at the level of the renal hilus with exophytic spread in the ventral and cranial directions (Fig. 5 and 6). The liver appeared to be impressed by the tumor mass. Caudally, tumor spreaded to the level of the lower renal lobe leaving a narrow parenchymal bridge at the level of renal hilus as the only connection with the kidney. The rest of the tumor seemed well separated from the renal cortex. The tumor mass was of lesser density when compared to the normal renal tissue.

Another smaller tumor of similar CT characteristics was found in the lower lobe of the left kidney. It contained a larger regular zone resembling a cyst. No signs of tumor calcifications were found. Renal veins seemed uninvolved. A small



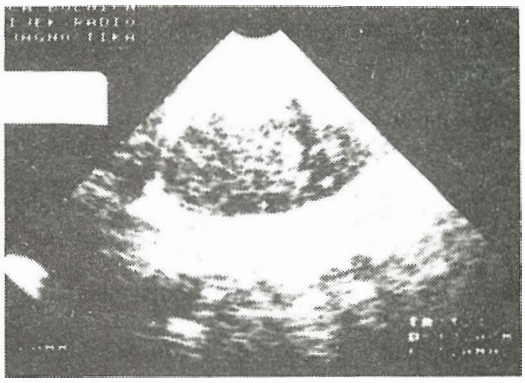
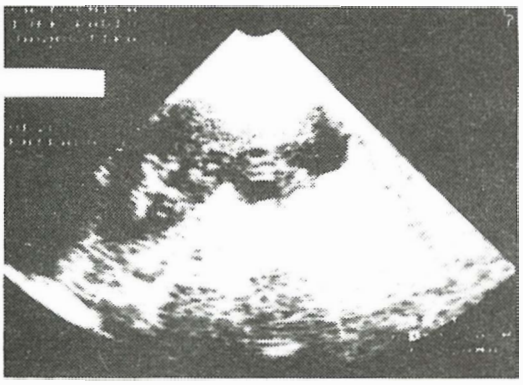


Fig. 1 and 2 – Right subcostal and coronar approach to the large hyperechogenic lesion in the upper lobe of the right kidney. Notice the small dark areas suggesting the spots of necrosis.



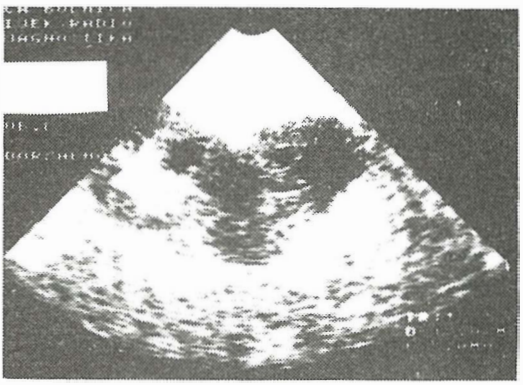
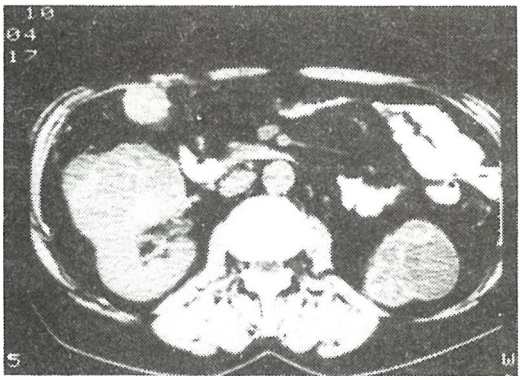


Fig. 3 and 4 – Coronar (Fig. 3) and dorsal (Fig. 4) approach to the smaller cystic tumor in the lower lobe of the left kidney.



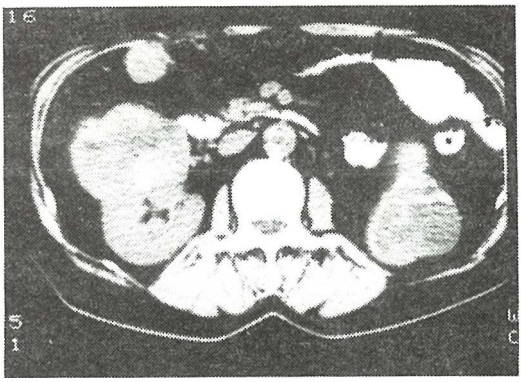
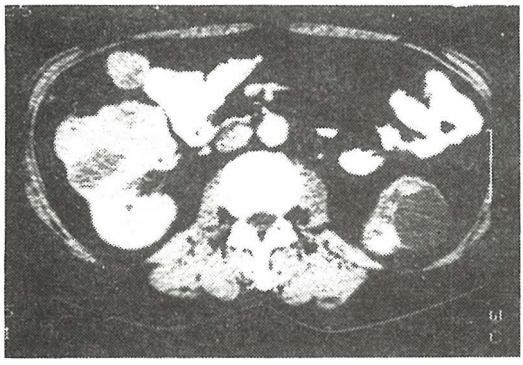


Fig. 5 and 6 – CT slices showing bilateral kidney tumors together with a metastatic lesion in the ventral part of the abdomen.



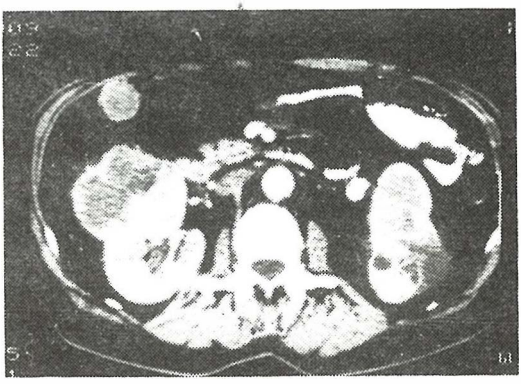


Fig. 7 and 8 – CT slices after contrast application. Notice iregular tumor opacity.

oval lesion of similar density was visible in the ventral part of the abdomen.

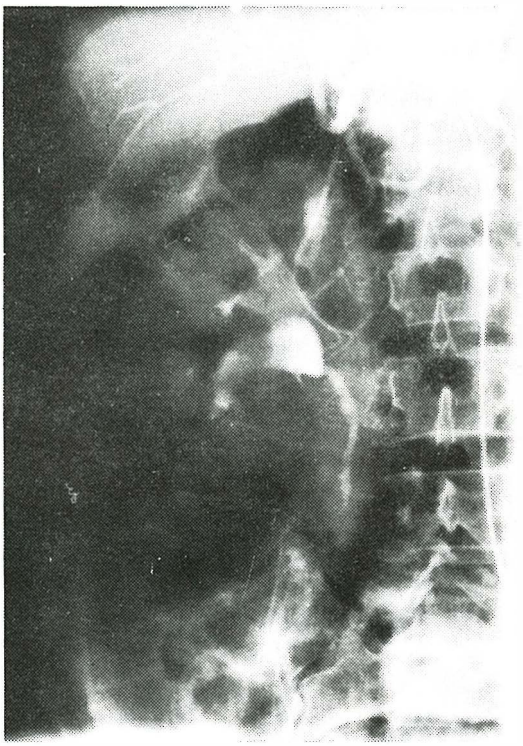
Twenty seconds after the contrast application, necrotic tumor centers showed no signs of opacification while the peripheral zone became highly opacified (Fig. 7 and 8). The border between two zones was fully irregular. The upper part of the tumor showed no clear distinction toward the liver. It was fully surrounded by liver tissue suggesting liver infiltration.

Prescheduled static renal scintigraphy showed diffuse cortical reduction of the right kidney with no signs of focal lesions. The left kidney was described as smaller because the lower lobe was not visualised. Previously planned urography was considered unnecessary and was therefore omitted. It was decided than angiographic procedures should be proceeded.

Angiographic evaluation started with general abdominal aortography followed by the selective left and right renal angiographies and selective celiac axis angiography. Seldinger technique was used with Telebrix 380 and 300 as contrast media.

Selective right renal angiography showed a well delineated hypervascular tumor 14 x 10 cm in the upper half of the right kidney. Numerous pathological blood vessels, irregular lakes of contrast and wide capsular arteries were noted. Left renal angiography showed scarce pathological vascularisation with few fine capsular arteries in the lower kidney pole. Late angiographic phase showed no tumor–like opacification. Both sides showed no signs of early venous drainage or pathological changes of the renal veins. Selective celiac axis angiography revealed no signs of pathological vascularisation of the right liver lobe.

After all findings were put together, ultrasound guided puncture of the larger and presumably malignant right kidney lesion was recommended on our radiological and oncological mee-



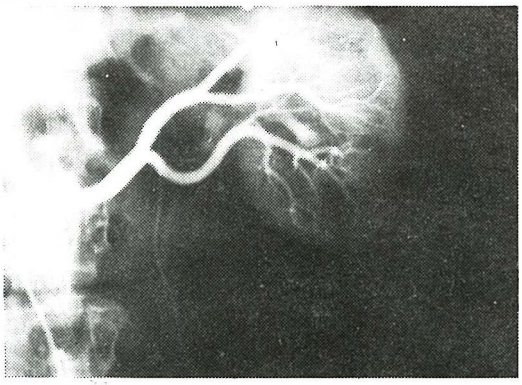


Fig. 9 and 10 – Right and left kidney selective angiographies.

tings. The patient preferred surgery and was transferred to the Department of Urology.

Total right and partial left nephrectomies were performed in a single act. Hystopathologically, both kidney tumors and a small abdominal focal lesion were renal cell carcinomas.

Discussion – Sinchronous renal cell carcinoma (SRCC) is usally regarded as extremely rare. SRCC and not–simultaneous or metachronous renal cell carcinoma (MRCC) are estimated to occur in 2 to 4 % of all renal cell carcinoma patients (2). One of the largest studies included 11 patients with bilateral renal neoplasms, six of them proven SRCC cases (2). Two patients out of 7 cases of bilateral renal tumors were renal carcinoma patients, both MRCC type (3). The post mortem studies revealed much higher percentages (4, 5).

When comparing diagnostic tools used to evaluate 99 focal kidney lesions (37 cysts and 56 carcinomas) ultrasound proved to be exact in 88%, CT in 96 % and selective angiography in 84% (6). Diagnostic modalities can and should be used complementary to solve complicated cases.

In the presented case, the first approach to the patient with nonspecific symptoms was made by abdominal ultrasound. It revealed a puzzling finding of bilateral massive kidney lesions that appeared ultrasonically different. It was followed by CT and angiography. Conventional urography was not done in the first place, because the patient had no signs of urinary troubles.

Differences between the tumors were obvious also on angiography. It verified the presence of a large hypervascular right kidney tumor, whereas the left kidney lesion finding was dubious because of extreme hypovascularity. On the contrary, both tumors showed very similar, if not identical CT characteristics (appearance, density, contrast opacity. An abdominal metastasis was found only by CT. Another valuable CT information was the irregular shape of te right kidney tumor necrotic zones. It was strongly consistent with tumor and not with an inflammatory process, although the clinical symptoms could be misleading. CT misguided us when it appeared that the right liver lobe was infiltrated by the tumor mass. Celiac axis angiography was normal and surgeons found that the intact liver capsule was only impressed by the kidney tumor.

It can be concluded that although ultrasound screening in our patient pathed the way towards the final diagnosis, CT, within its limits, proved to be the most useful when comparing two lesions and estimating the extent of disease.

Cases of SRCC and MRCC are usually understood as an early or late metastasis in the opposite kidney (1,2,8). It is difficult or often impossible to distinguish bilateral primary tumors from a contralateral metastatic tumor. In the presented case, we were unable to solve this

problem. Both lesions might have been the primary tumors. The greater right kidney tumor with dominant necrotic areas did not contain cysts. In the smaller and cystic tumor of the left kidney necrotic areas were not so abundant. The first three criteria proposed by Hyman et al (9) to identify primary bilateral kidney tumor were fulfilled. Both tumors seemed simulataneous and each kidney contained only one encapsulated tumor. But, histologically both tumors were similar, thus suggesting to be of the same origin.

Sažetak

ISTOVREMENI OBOSTRANI KARCINOM BUBREGA EVALUIRAN SA UZ, CT i ANGIOGRAFSKI

Prikazan je bolesnik s istovremenim obostranim karcinomom bubrega. Kompjuterizirana tomografija, angiografija i ultrazvuk su se pokazale komplementarnim dijagnostičkim modalitetima sa sopstvenim ograničenjima.

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FROM PRACTICE FOR PRACTICE

CARDIOVASCULAR SYSTEM
Case 3

What is this investigation? What abnormalities does it show? What further investigation(s) would you perform? What therapeutic options are available to deal with the main abnormality shown?

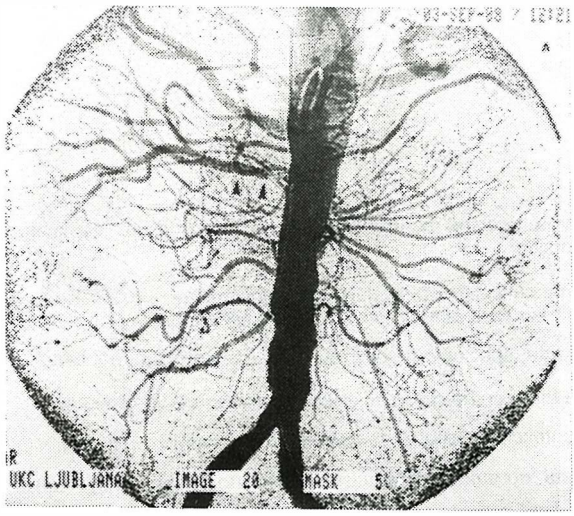

Fig. 1a

For answers see page 240

SANOLABOR

Izvozno uvozno podjetje
za promet z medicinskimi instrumenti, aparati,
opremo za bolnice, laboratorije in lekarne

LJUBLJANA, Cigaletova 9
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Iz prodajnega programa trgovine na debelo nudimo široko izbiro domačega in uvoženega blaga po konkurenčnih cenah in sicer:

- rentgenske filme in kemikalije proizvajalcev »Fotokemika«, »KODAK«, »3. M – TRIMAX«, »AGFA GEVAERT« in drugih ter kontrastna sredstva firme »NICHOLAC«,
- medicinske instrumente, specialno medicinsko in sanitetno blago, potrošno blago za enkratno uporabo,
- medicinske aparate in rezervne dele zanje ter bolniško in drugo opremo,
- tekstilne izdelke, konfekcijo in obutev za potrebe zdravstvenih, proizvodnih in varstvenih organizacij,
- laboratorijske aparate, opremo, laboratorijsko steklovino, reagente, kemikalije in pribor,
- aparate, instrumente in potrošno blago za zobozdravstvo.

V prodajalni na Cigaletovi 9 v Ljubljani prodajamo izdelke iz asortimana trgovine na debelo, s posebnim poudarkom na blagu za zobozdravstvo, nego bolnikov, ortopedskih pripomočkih in ostalemu blagu za široko potrošnjo.

UNIVERSITY HOSPITAL »DR. MLADEN STOJANOVIĆ«, ZAGREB
DEPARTMENT OF NUCLEAR MEDICINE AND ONCOLOGY

MODEL FOR COMPUTER SIMULATION OF MULTIPINHOLE THALLIUM–201 HEART IMAGING

Lokner V

Abstract – Seven pinhole collimator was modeled as a simple non-multiplexed form of multipinhole imaging system. The aim of modeling is computer simulation of imaging and generation of artificial images that can be used for controlled testing of image processing algorithms as well as optimization of parameters. For thallium-201 heart imaging, physical model is described as well as corresponding mathematical model used as formal framework for computer implementation. The image generator works with the heart-phantom, simulating formation of no-noise image. Poisson noise is added to the image later on. The image normalized to 100 counts/pixel maximum and 620,000 total counts was generated with the average signal to noise ratio of 6. Image frequency properties are identical to those found on standard clinical nuclear medicine images. Further application of modeling on various types of apertures and/or objects is possible as well as addition of other image degrading mechanism.

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Key words: heart-radionuclide imaging; image processing, computer–assisted

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Introduction – Nuclear medicine (NM) images are of poor quality and therefore difficult for clinical interpretation due to deficient resolution and insufficient contrast discrimination. Main sources of image degradation are blur and Poisson type of noise. Diagnostic assessment from clinically obtained NM images could be improved via image processing (1). There is no unique way for quality upgrade through image enhancement or restoration. Various design strategies for processing algorithms were tested and increase of detectability and contrast discrimination verified by receiver operated characteristics (ROC) was reported (2-5). However, proficiency testing of different numerical techniques for processing and their computer implementation is indicated and related to arbitrary definitions of optimality.

Our study is focused on the model formulation for simple NM imaging system. The aim of modeling is computer simulation of imaging and generation of artificial images that can be used for controlled testing of processing algorithms as well as optimization of parameters. Such a model as well as corresponding simulated images are especially needed if noise suppression techniques are investigated.

Seven pinhole (7P) collimator with standard large field of view (LFOV) gamma camera is chosen to be modeled as non-multiplexed form of multipinhole imaging system (6-8). Physical model of thallium-201 heart imaging is described as well as corresponding mathematical model used as formal framework for computer implementation of image generator.

Physical model of imaging (Theory) – In nuclear medicine the object (spatial distribution of radionuclide) and the image is complex and non-linear due to stohastic properties of decay process, absorption and scatter through the body and intrinsic non-linearity of detector. Linear model of imaging could be constructed as useful approximation of such a system. Under certain imaging conditions (e.g. gamma camera count rate less then 50K counts/s (9) and with some supplementary assumptions, linearity supposition is justified. We postulate that:

- object is a source of isotropic and time stationary radiation with so small a wavelength that physical optics phenomena (e.g. diffraction) are disregarded;
- noise is related to stohastic processes and of Poisson type;

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• absorption is continuous and with known absorption coefficient; there is no scattered radiation;

• aperture plate is ideally thin with zero transmittance everywhere except on the openings;

• detector is ideally linear and uniform, with unit efficiency.

Since Poisson noise is additive and of constant mean value (10), modeling could be separated in two steps: in the first one, blurring model will be considered; in the second, model of direct noise addition to the image will be introduced.

Blurring model : Blur is limited to geometry distortion only so that linear deterministic model of imaging is:

$$I(x,y) = \int_{\infty} T(x,y,x',y',z')\, O(x',y',z')\, d(x',y',z') \quad [1]$$

where (x,y) are the detector plane coordinates; (x',y',z') are the spatial coordinates above the aperture plane; I(...) is the image; T(...) is the system transfer function (TF); O(...) is the object function. Eq [1] is still far too complicated for practical purposes. In order to calculate image, full specification of TF is needed. Since this is not readily available, further approximations are necessary. Imaging models could be solved only individually, using supplementary, problem specific, simplifications.

We will bound our interest to a special case of multipinhole apertures. Point spread function (PSF) for such systems is quite simple but neveretheless, since pinhole systems are space variant, full knowledge of TF is still needed. If the object size is small compared to the aperture plane/detector plane distance, and/or the pinhole size is small, so that $T(x,y; x',y',z') \approx T(x-x',y-y'; z')$, the system could be considered as isoplanatic or shift invariant for limited areas (1). For such isoplanatic patches, eq [1] could be transformed into convolution integral and the model of imaging simplified considerably. If the object slice is taken parallel with the aperture plane, and then projected through the center of a pinhole onto the detector plane, the sharpest possible image is formed to which we will give a special name – zerohole projection. The image of an object through aperture of finite (nonzero) dimension could be understood as being an integral over all slice images, which are zero-hole projections of particular slices convoluted with corresponding PSF.

Computer implementation requires that continuous form of model equations should be adopted. We will outline here only the ideas of discrete description of the imaging system. Half-space above the aperture, plane is divided into parallel slices which are subdivided into voxels. It is assumed that all the activity is concentrated in the center of the voxel. Since our interest is bounded to the limited part of the space, there are K slices only, each of them with a total of M_K voxels. The image is a square matrix divided into pixels. Eq.[1] in a discrete form reads (1).

$$I(x,y) = P \sum_{k=1}^{K} \sum_{m=1}^{M_K} \frac{\Delta V^k}{Z_k^2}\, O(x_{mk}, y_{mk})\, A(x_{mk}, y_{mk}, x, y)\, \cos^3 O(x_{mk}, y_{mk}; x, y). \quad [2]$$

(x,y) are the coordinates in the center of a pixel; (x_{mk},y_{mk}) are the center of the m-th voxel, the k-th slice coordinates, z_k from the surface of the detector; P is the pixel area; ΔV_k is the voxel volume; $O(x_{mk},y_{mk})$ is the emission function; $A(x_{mk},y_{mk}; x,y)$ is the aperture function; $O(x_{mk},y_{mk};x,y)$ is the angle between voxel to pixel ray and system axis. If imaging is non-multiplexing and small enough to be considered as isoplanatic, we can recognize that all the rays contributing to one image pixel, pass through the same pinhole, so that to a good aproximation, $O(x_{mk},y_{mk}; x,y) \approx O(x,y)$. Nearly shift invariant multipinhole imaging system could be transformed to exactly shift invariant system by scalar $\cos^3 O(..)$ scaling of the image matrix. For the described model, one of the image generation algorithms is:

• for a given slice, choose a voxel; find pixels where geometrically defined rays (center of the voxel/centers of the pinholes) intersect with the detector plane; add corresponding values of the intensity;

• next voxel;

• if all the voxels in a slice are projected, the zero-hole image of the slice is generated; add this image to the zero-hole projection image matrix; calculate PSF for the slice; make fast Fourier transforms (FFT) of the zero-hole image of the slice and PSF; multiply them to perform convolution and with inverse FFT return the

result to the spatial domain; add the transform to the image matrix;

- next slice;
- using $\cos^3$ O(x,y) scaling adjust the image to shift-variant conditions.

Noise generator : Since noise is Poisson distributed, additive, with a constant variance and uncorrelated to the object (10), noise addition to the image could be done on a pixel by pixel basis. Poisson random number generator produces series of values having the initial pixel intensity taken to be the mean of distribution (12). Different image noise levels are regulated by predefined range around the mean, using variance as measure; for a given pixel, a sequence of random numbers is repeated until one is found laying inside the given limits. Signal to noise ratio (SNR) is the local (pixel) property for all NM images. Describing the image as a whole, SNR could only be approximated as the mean noise level being equal to the sqaure root from the pixel mean value, in accordance with the definition.

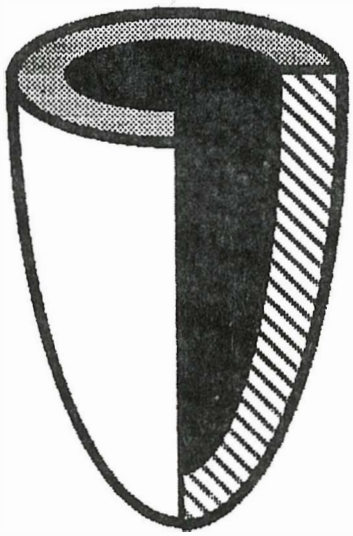

Fig. 1 – Two half-ellipsoids, one inside another with the coinciding long axes, were used as outside and inside surfaces of numerical heart-phantom: long axes are 105 mm and 120 mm; both short axes are equal, and 25 mm and 45 mm, respectively.

Model parameters and simulation – 7P collimator was chosen to be modeled as a simple non-multiplexed form of a multipinhole imaging system.

System geometry : The aperture plane is parallel with the detector surface which is circular having 380 mm effective diameter. The distance between the detector plane and the aperture plane is 127 mm. Seven circular pinholes (7 mm diameter) are arranged in hexagonal pattern in such a way that system axes coincide with one pinhole, while 6 of them are circularly distributed on a 63.5 mm distance. The seven object projections are non-overlapping owing to the septa placed the between adjacent pinholes.

Pixels and voxel : All the images in this study are represented with a 128x128 matrix so that every pixel coers 3x3 mm^2 of the detector surface. All voxels are having equal base 2x2 mm^2 and increasing slice and voxel height from 4 to 16 mm, depending on Z_k.

Phantom object : Hollow half-ellipsoid represents a heart-like object (Fig. 1). The phantom object is placed above the central pinhole in such a way that object's long axes coincide with the system axes (Fig. 2). The body contour is simulated with the oblique plane that makes 15° and 30° angles with x and y axes, respectively. All body voxels (voxels inside body contour) are emitting in accordance with heart tissue/surrounding tissue and heart tissue/blood ratios that are approximately 3:1 for thallium-201 in equilibrium few minutes after injection (13). Assuming homogeneous tissue, for $E_\gamma \cong 167$ keV, absorption coefficient for water $\mu = 0.02\ cm^{-1}$ was used. For voxels more than 332 mm above the detector surface, absorption is so high that their effect on the image could be wholly disregarded. All the rays originating in a particular voxel and passing through a given pinhole are equally absorbed.

Data generation : Simulation was done using IMB–3083–JX1. Programmes were written on FORTRAN utilizing IMSL library for FFT routines. For a single image 2.5×10^9 operations 128x128 matrix are needed. With 2 MIPS, the generation of a single image takes 10 min of processor time.

Results – Simulated heart-phantom image was normalized to 100 counts/pixel maximum, resulting in $\simeq$ 620,000 total counts that is the standard value for clinical images of the same type. The image contains 7 object projections (Fig. 3). Pixel values in the part of the image matrix outside 7 projections of pencil shaped simultaneous field of view (SFOV) were intentionally set to zero. This part of the image contains incomplete information on object space voxels. Two variances widths was used as a bounding criterion of acceptable values for noise generator dissipation. Total number of counts on the image, after random noise generator, changed for less than 0.08%, proving that noise model is correct

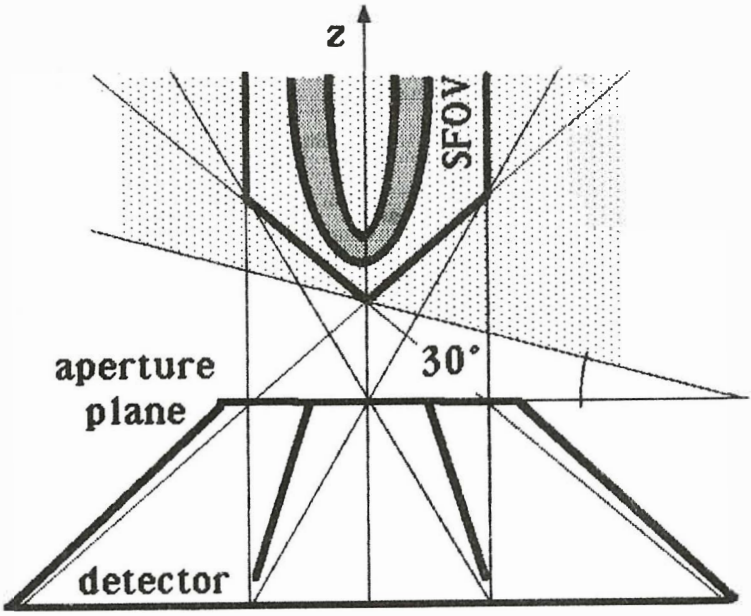

Fig. 2 – A cut through model: 7 pinhole collimator is indicated with positions of three visible pinholes; the heart phantom is placed along the system axes, inside SFOV, with it's top 332 mm above the detector plane; shaded area represents body tissue absorbing medium with lower thallium-201 concentration.

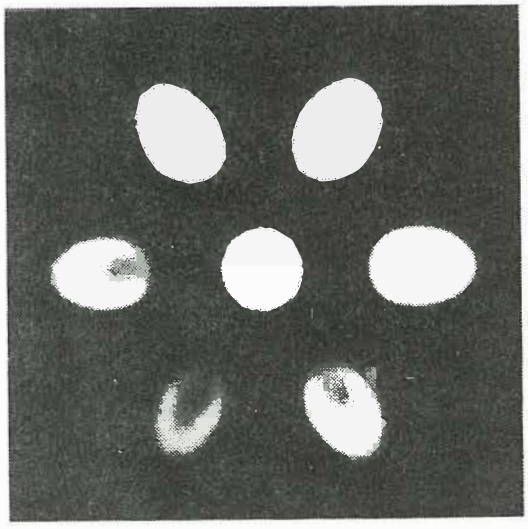

Fig. 3 – The artificial heart phantom image without noise: 7 different heart projections are visible after background has been subtracted to stress the differences in absorption due to the oblique body contour.

and that random noise generator was working appropriately. With approximately 60 counts per non-zero pixel, image average SNR is $\simeq$ 6 (Fig. 4).

Image spectral properties were analyzed in the frequency space. For that purpose the additional image was calculated as a pixel by pixel difference of two matrices: one geometrically degraded without noise and a corresponding one with randomly added noise. After 2D Fourier transformation of all three images, their symmetrical power spectrum was calculated. In order to compensate for local fluctuations, 2D power spectra was compressed to 1D by averaging in frequency domain over annuli (average of all the values with the same frequency vector). The results are plotted in Fig. 5. All the power spectrum properties are similar to those reported earlier for clinical images of different object and total number of counts (2,3).

Discussion – A practical model of multipinhole imaging could be constructed, computer implemented and used in simulation studies to

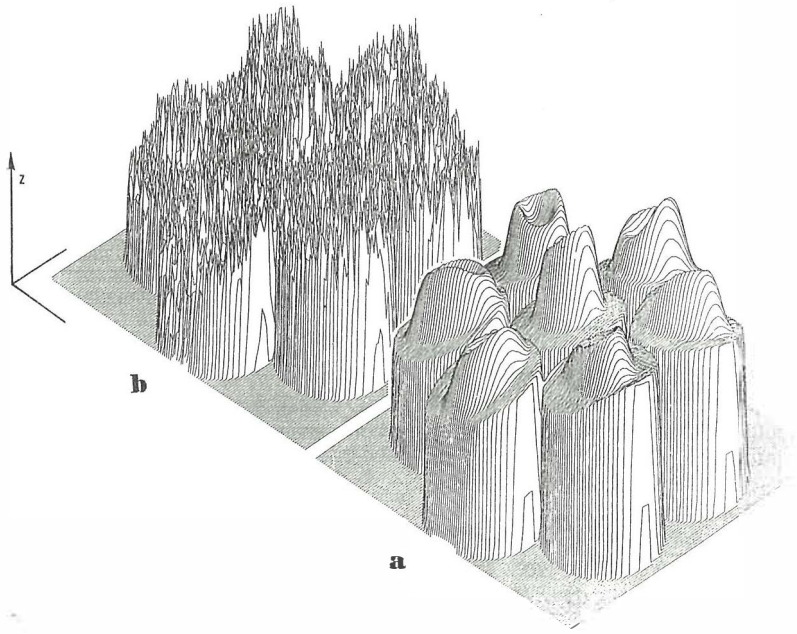

Fig. 4 – (a) Pseudo the 3D display of the simulated image in Fig. 3. z-axes represents the number of counts in pixel. The background is visible. (b) Same image after Poisson noise was added.

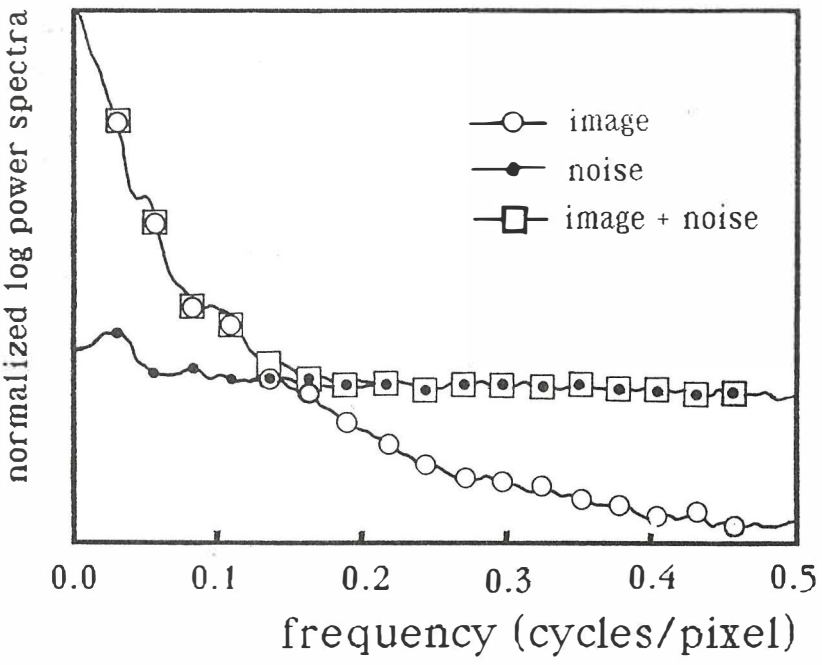

Fig. 5 – Normalized power spectrums for three images of the heart phantom: (a) the simulated image (image); (b) same image with added Poisson noise so that average SNR $\simeq$ 6 (image+noise); (c) image formed as difference between the first two images (noise). The power spectrums are »compressed« to one dimension by averaging over annuli in the frequency domain. The noise amplitude is having constant value over all frequencies.

generate sets of images. Artificial images meet frequency properties found on standard clinical images of the same type. The ease of image generation control through parameter changes make such models convenient for image processing studies because of possibility to tailor the structure of the image to a particular task, either through simulation of sharp (zero-hole projection) images, noise free images or images with controlled level of Poisson noise. By the same token, various numerical experiments could be performed on the heart-phantom by simulating regional perfusion distrubances of different sizes. Image analyses could be used for testing relation between location and size of low thallium-201 intake and corresponding changes (defect resolution) on simulated image. Also, some new types of phantom objects (e.g. thyroid) or degrading mechanisms (e.g. Compton scattering) could be incorporated to basic model. Modeling and simulation approach demonstrated in this work offers more posibilities than previously used low-pass filtering and scaling of measured high total count rate images of phantoms (3).

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Sažetak

MODEL ZA KOMPJUTERSKU SIMULACIJU MULTIPINHOL OSLIKAVANJA SRČANOG MIŠIĆA TALIJEM-201

Sedam pinhole kolimator je modeliran kao jednostavan oblik sustava za oslikavanje bez prekrivanja projekcija. Cilj modeliranja je računarska simulacija oslikavanja generiranjem umjetnih slika koje se mogu koristiti za kontrolirano testiranje algoritama za obradu slike kao i optimizaciju parametara. Za oslikavanje srčanog mišića s talijem-201 opisan je fizikalni model kao i njemu odgovarajući matematički model koji se koristi kao formalni okvir implementacije na računaru. Generator slika radi sa fantom-objektom oblika srčanog mišića simulirajući formiranje slike bez šuma. Poissonov šum je kasnije dodan slici. Slika je normalizirana maksimum od 100 impulsa/pikslu tako da ima 620,000 impulsa ukupno sa prosječnim omjerom signala i šuma koji iznosi 6. Frekvencijska svojstva slike su identična onima koja se nalaze na standardnim kliničkim slikama u nuklearnoj medicini. Moguća je daljnja primjena modeliranja na različite tipove apertura i/ili objekata kao i uključivanje drugih mehanizama degradacije slike.

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MICROVASCULAR FREE FLAPS IN RECONSTRUCTION AFTER ABLATIVE SURGERY OF HEAD AND NECK TUMORS

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Abstract – In the reconstructions after extensive ablative surgery for head and neck carcinomas microvascular free flaps (MFF) have shown several advantages over pedicled flaps, particularly in preoperatively irradiated patients, and therefore they represent the method of choice in this type of surgery. During the years 1985-1990, MFF were used in 28 patients treated at the University Department of Otorhinolaryngology and Cervicofacial Surgery in Ljubljana; of these, 10 had recurrent carcinoma of the facial skin, and 18 carcinoma of the oral cavity and oropharynx. Reconstruction of the mandible was performed in 5 patients with carcinoma of the floor of the mouth, in two cases by means of an osteocutaneous flap of the iliac crest, whereas in another two a radial forearm flap and in one case a scapular flap were used. For reconstruction of the skin or mucosa radial forearm flaps were used most frequently, but apart from these, upper forearm flap and latissimus dorsi flap were used as well. As to the duration of surgery, hospitalization time and the rate of complications, our results are comparable with those reported in the literature.

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Key words: head and neck neoplasms-surgery;surgical flaps

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Introduction – The treatment success in advanced head and neck tumors is greatly dependent on the extent of excision with convincing safety margins, which is primarily influenced by the possibility of related defect reconstruction. In comparison with other sites, extensive ablative surgical interventions in head and neck tumors result in more severe cosmetic and functional deformities. The ideal method of reconstruction of defect in this area should be a reliable and final one; with respect to the specificity of the treated site, it should offer a wide range of possibilities to achieve the optimum functional and cosmetic results. Of the numerous procedures available, the microvascular free tissue transfer most closely complied with the above requirements.

After the initial laboratory experiments performed already in 1908 by Carrel (1), this surgical technique had been abandoned all until the 70's when it was again brought to attention. The first report on a successful microvascular skin transfer was published in 1973 by Taylor and Daniel (2). The intraoral use of free skin flaps was introduced by Panje et al in 1976 (3) and Ackland and Flynn in 1978 (4), whereas the first mandibular microvascular reconstruction was reported in 1977 by Serafin et al (5); in 1983 excellent results obtained by the use of radial forearm flap were reported by Soutar et al. (6). At the University Clinical Center in Ljubljana the routine use of microvascular surgical technique was started in 1975 by Godina (7).

In the last two decades, several different flaps have been introduced for microvascular transfer. The selection of flap depends on the tissue to be substituted, e.g. the skin or mucosa alone, or deeper defects should be reconstructed including a missing bone. So, groin flap, dorsalis pedis flap, latissimus dorsi flap, scapular flap, radial forearm flap and lateral upper arm flap have been introduced for skin and mucosa replacement, whereas rib, iliac, scapular, metatarsal, as well as radial and lateral upper arm flap are used in osteomyocutaneous reconstructions (8).

Clinical data – In the years 1985-1990, reconstruction of extensive defects after ablative surgery of head and neck carcinomas by means of microvascular free flap (MFF) was performed in 28 patients treated at the University Department of Otorhinolaryngology and Cervicofacial Surgery in Ljubljana. Selection of MFF for various recipient areas is presented in Table 1.

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Table 1 – Selection of flaps for reconstruction of deffects after ablative cancer surgery in patients, treated at University Department of Otorhinolaryngology and Cervico–Facial Surgery in Ljubljana in the years 1986-1990

Recipient area / Selected flaps	Facial skin	Oral cavity	Pharynx	Total
Radial forearm flap	7	7	5	19
Lateral upper arm flap	3	1	–	4
Latissimus dorsi flap	–	–	2	2
Iliac osteocutaneous flap	–	2	–	2
Scapular osteocutaneous flap	–	1	–	1
TOTAL	10	11	7	28

All 10 patients with facial skin carcinoma had recurrent disease after previous unsuccessful surgery and/or radio-therapy performed in other institutions. Besides an extensive cutaneous and subcutaneous tissue excision, 4 patients also underwent exenteration of the orbit, whereas 2 had simultaneous ethmoidectomy and 3 patients had partial resection of the nose due to tumor invasion into the nasal cavity. Facial artery and vein were used as recipient vessels in 7 cases, and in 3 flaps the anastomoses were performed with superficial temporal vessels.

All except four patients with carcinoma of the oral cavity and oropharynx, in whom the treatment was a primary one, had recurrent disease after previous surgery and/or radio-therapy. The decision for reconstruction of the mandible with an osteomyocutaneous flap was made in 5 patients with carcinoma of the floor of the mouth. Osteocutaneous flap of the iliac crest was used in two cases, a radial forearm flap in another two, and a scapular flap in one case. For microvascular anastomoses the superior thyroid artery, lingual artery, facial artery, and the external or common carotid arteries were used as donor vessels; in the latter cases end-to-side technique was performed.

Each surgery required cooperation of two teams: one for ablative head and neck procedure and the other for reconstructive plastic surgery. The duration of surgery ranged from 5 to 13 hours, mean 7.5 hours. The patients were hospitalized for 17-64 days, mean duration of hospitalization being 37 days.

Flap necrosis occurred in two cases: in one patient with MFF of the iliac crest the non-viable transplant was removed after three weeks, whereas in the other one necrosis of the radial forearm flap used for pharyngeal reconstruction occurred on the second day after surgery; the defect was subsequently covered using a pedicled pectoral myocutaneous flap. There were 2 minor oro- or pharyngocutaneous fistulas; these, however, healed spontaneously after 14 and 21 days respectively.

Discussion – The use of MFF in reconstruction following ablative surgery of head and neck tumors has a considerable advantage over pedicled flaps. Namely, the length and the width of the latter flap are limited, and its tip is frequently insufficiently vascularized since the distal part of a pedicled flap often reaches beyond the natural margins which still receive satisfactory blood supply from the pertinent blood vessels. In contrast with that, MFF represents a central area of arterial and venous blood supply. MFF provides a sufficient amount of well vascularized tissue which renders reconstruction of practically every defect feasible. The very size of MFF frees ablative surgeons of the eternal dilemma how to remove the whole tumor with sufficient safety margin, i.e. in accordance with oncological principles, and at the same time maintain the possibility of having the defect satisfactorily reconstructed from both functional and aesthetic point of view. MFF also meets the most essential requirement of present oncological surgery according to which the final reconstruction should be immediate, with a relatively short hospitalization time; all this is of particular importance for patients with extensive malignomas of the head & neck region. The hospitalization time of our patients does not differ from that reported in the literature (4).

On the other hand, we should be aware of certain drawbacks of MFF reconstruction. The surgical procedure is longlasting and requires specially skilled surgeons. In our interventions, generally, both surgical teams performed their work simultaneously, which explains shorter duration of surgery in comparison with those reported by other authors (8,9,10,11). It should be stressed that these operations require a microvascular surgeon who handles free-flap transfers in his routine clinical work to minimize the rate of complications and to shorten the duration of surgery (12). In the case of unsuccessful flap transplantation, the loss of MFF is complete in contrast to a pedicled flap where only its distal

part is lost. Therefore the flap should be monitored every hour during the first postoperative days to allow for immediate revision in case of thrombosis of the vessels (7,12). In our patients revisions were required in 4 cases of which 3 were successful.

The decision which of the available MFF variants will be selected in a particular case depends on whether only a thin layer of lining is needed, or the flap should replace a bulk of tissue or even reconstruct a missing part of the bone. Last but not least, this decision is influenced also by the microsurgeon's skill and his preference for a particular flap type. It was mainly for the latter reason that of 21 flaps needed for reconstruction of facial skin defect, part of the oral cavity and pharynx, in as many as 17 cases we chose the radial forearm flap instead of the lateral upper arm flap which is equally suitable for reconstruction, but entails significantly less apparent mutilation of the donor site.

We rarely performed reconstruction after segmental mandibulectomy, believing that only resection of the front part of the mandible represents an absolute indication for reconstruction, due to the entailed surgery-related difficulties at swallowing and articulation as well as severe aesthetic sequels which the patient might find unacceptable. Namely, our experience, as well as that of other authors, show that the resection of the mandibular ramus in comparison with the resection of its frontal part does not cause excessive functional and cosmetic defects (11). Among the available combined osteomyocutaneous flaps those taken from the iliac crest, forearm and scapula were selected. Of the three, the latter flap appears most suitable due to excellent vascularization of the skin and bone, as well as due to great mobility of the skin from the related bone, which has given a very good result also in our patient (Fig. 1). The only drawback of this reconstruction method is in the long duration of surgery. Particularly in reconstruction of the mandible, the technique of microvascular transfer proved most suitable since the percentage of successful reconstruction outcomes using osteomyocutaneous pedicled flaps had not been satisfactory. Also the use of alloplastic implants has generally been disappointing; this applies specially to irradiated tumor beds where sufficient vascularization of the transplant is of particular importance (9, 13, 14).

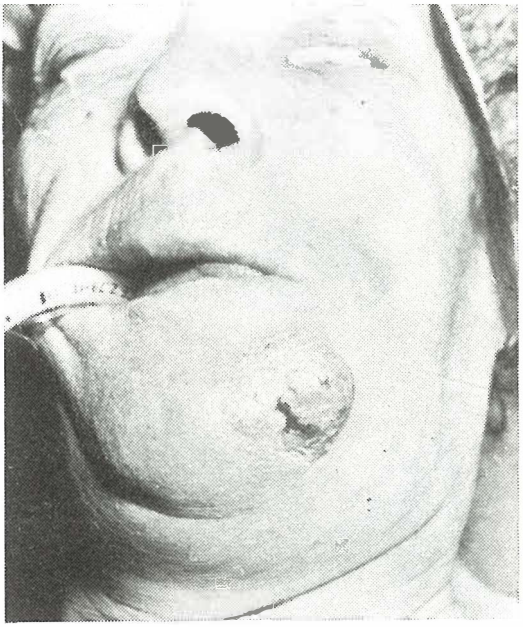

Fig. 1a – Patient with advanced carcinoma of the floor of the mouth infiltrating through the mandible into the skin

End-to-end and end-to-side techniques for anastomoses were used in almost equal proportion. Although, by some authors, the end-to-side technique is used only in exceptional cases when there are no branches of the carotid artery available, we have found this technique even more successful and by all means safer (12, 15).

Our series of recurrent skin carcinomas points out again that, regardless seemingly limited extent of tumor, the primary treatment of such malignomas should be carried out in accordance with all principles of oncological surgery. This is particularly true of prognostically unfavourable sites such as the nasal canthus and nasolabial sulcus. Namely, the very recurrences of these sites, particularly in the cases of basocellular carcinomas, may entail such severe mutilations as in our cases when exenteration of the orbit or removal of a large part of the nose was required (Fig. 2). The defect after excision is regularly larger than expected. Considering their aforementioned properties, this is also why microvascular flaps in such reconstructions have significant advantages over other methods. Verification of resection margins by frozen section method, which is routinely used in oncological surgery, should become part of regular practice not only in the surgery of extensive malignomas,

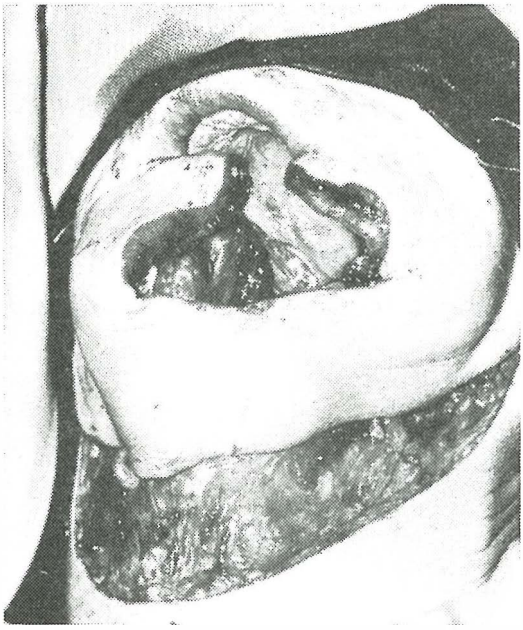

Fig. 1b – Defect after excision of the anterior part of the floor of the mouth together with symphysal segment of the mandible and adjacent skin

Fig. 1c – Dissected scapular osteocutaneous flap providing bone and the lining for both, floor of the mouth and skin

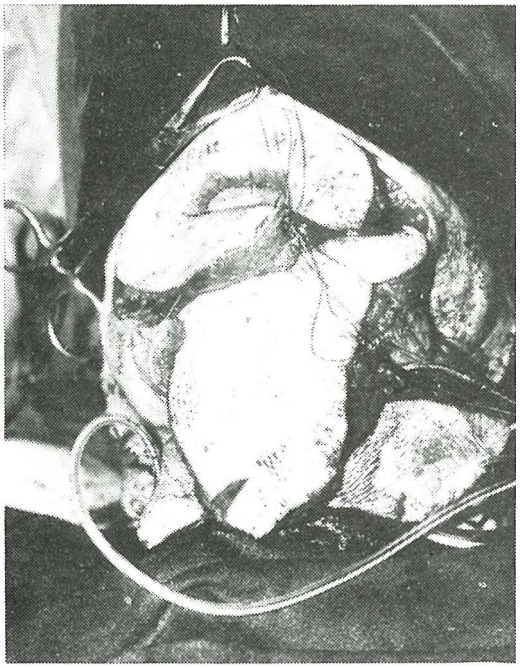

Fig. 1d – Reconstruction of the anterior part of the floor of the mouth and mandible is followed by reconstruction of skin defect.

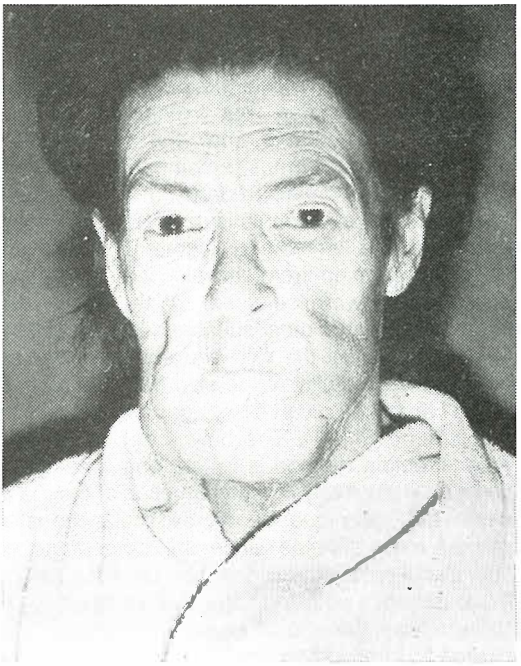

Fig. 1e – Patient one year after reconstruction with good cosmetic and functional result.

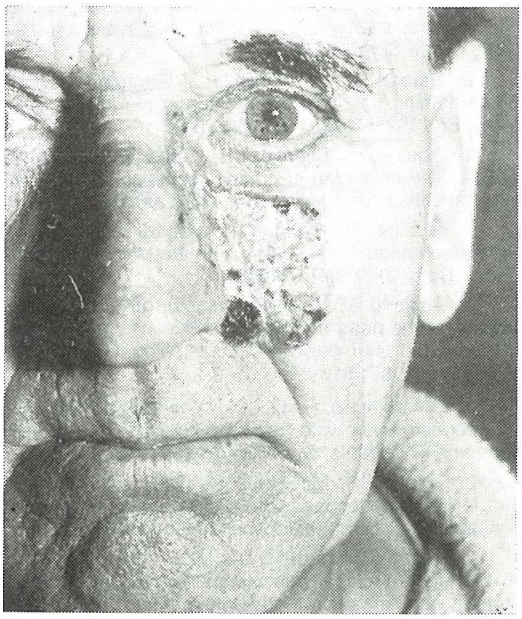

Fig. 2a – Recurrent basal cell carcinoma of the face after previous excision and radiotherapy.

Fig. 2b – Extensive defect after tumor excision

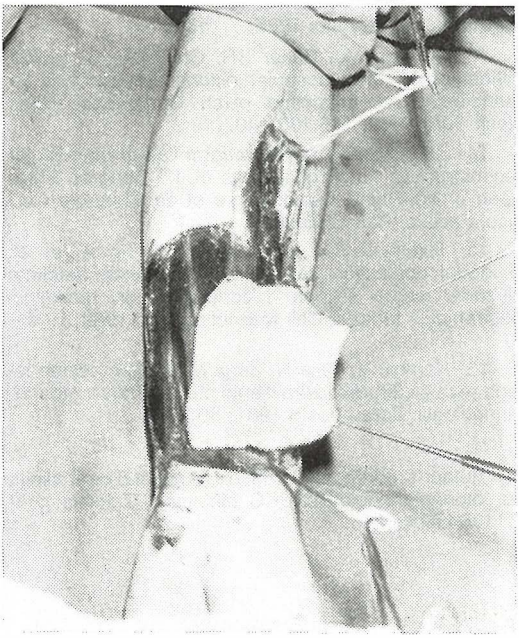

Fig. 2c – Radial forearm flap is elevated.

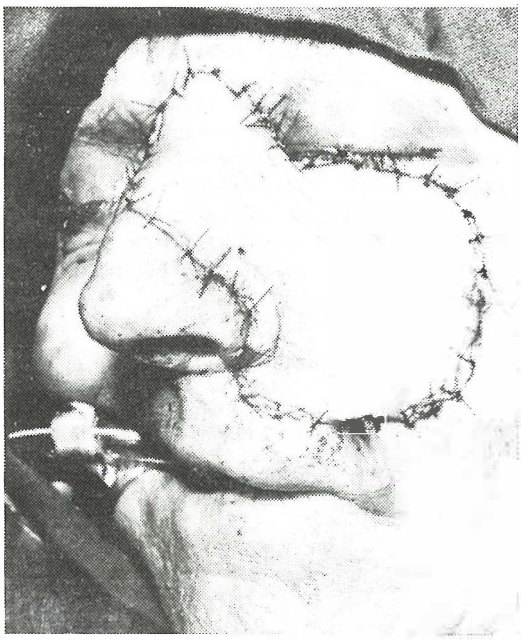

Fig. 2d – After completition of the vascular anastomosis to the facial artery and vein the flap is sutured into the defect

but first of all in every primary surgical treatment (16). Only by such an approach recurrences and related mutilating surgical procedures could be avoided.

Conclusions – In the reconstruction surgery after ablation of head and neck malignomas MFF have proved to have so many advantages over

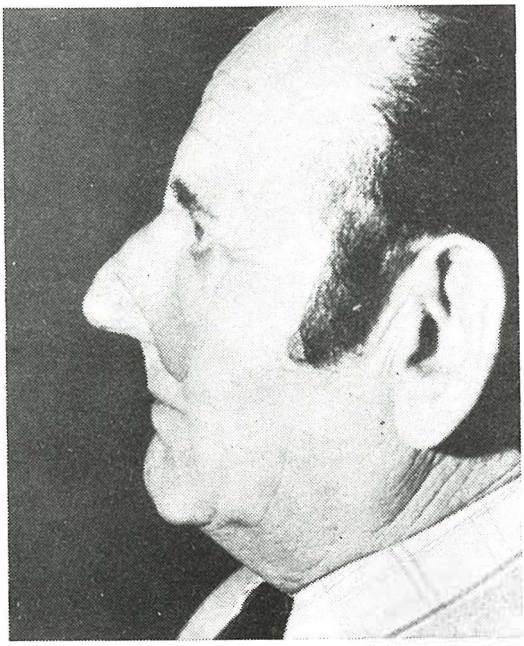

Fig. 2e – Patient one year after reconstruction

pedicled flaps that they should be regarded as the method of choice in such surgical interventions. This applies particularly to recurrences after previous unsuccessful treatment, which require reconstruction with an extremely well vascularized flap, and specially to bone transplants in reconstruction of the mandible.

Double-team approach using highly qualified surgeons shortens the duration of operations and results in a decreased rate of complications.

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COMPARISON OF TUMOR–ASSOCIATED TRYPSIN INHIBITOR (TATI) AND TISSUE POLYPEPTIDE ANTIGEN (TPA) IN SERUM AND PLEURAL EFFUSION IN PATIENTS WITH LUNG DISEASES

Lazarov A[1], Plavec G[2], Odavić M[1], Dangubić V[2], Koljević A[1]

Abstract – The concentration of tumor–associated trypsin inhibitor (TATI) was measured in serum and pleural effusion in 70 patients with malignant and nonmalignant lung diseases. The levels of TATI were compared with serum level of TPA in the same groups. Serum and pleural effusion TATI levels were determined by the immunoradiometric assay, using a commercial kit SPECTRIA TATI (Farmos Diagnostica). The levels of TPA were measured using the PROLIFIGEN TPA two–site immunoradiometric assay. Serum TATI and TPA levels were higher in malignant than in nonmalignant diseases. Concentrations of TATI in serum and pleural effusion showed a high correlation. Pleural effusion TPA was about 10–fold higher than serum TPA in the same patients. Sensitivity, specificity and accuracy were satisfactory for both TATI and TPA.

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Key words: lung diseases; tumor markers, biological; trypsin inhibitors

Orig sci paper

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Introduction – Tumor markers are used to help in the diagnosis and monitoring of tumors. No marker with defined specificity and sensitivity for early prediction of metastases at a subclinical stage has been identified. A new marker which has been introduced recently, is tumor–associated trypsin inhibitor (TATI). TATI is a small peptide (6000 dalton) which consists of 56 aminoacids and no carbohydrates. It has been isolated for the first time in the urine of women with ovarian carcinoma (1). High concentrations of TATI have been found in the urine of patients with gynaecological cancers (2), in the serum of patients with cancer of the pancreas and in those with chronic pancreatitis (3). High levels have been found in patients with cancer of the stomach and hepatoma (4). Very high levels of TATI also occured in the cyst fluid of patients with mucinous ovarian tumors (5).

Tissue polypeptide antigen (TPA) is another potential marker in lung cancer. High sensitivity and specificity were obtained in 44 patients with lung cancer (6).

TATI was compared with other tumors markers (CEA, CA 19-9, CA 50 and elastase) in patients with various gastrointestinal disorders and elevated levels of those markers were reported (7). TATI was also compared with other tumor markers such as CA 15-3, CA 125 and CA 19-9 (5, 8) in ovarian cancer.

In this study the concentrations of TATI were studied in serum and pleural effusion of patients with malignant and nonmalignant lung diseases. The levels of TATI were compared with serum levels of TPA in the same group of patients.

Materials and methods – The study comprised 70 patients; 51 of them were with malignant and 19 with nonmalignant lung diseases (table 1). Their age ranged from 37 to 80 years, mean age being 58.8 years. Forty–two healthy blood donors served as a control group. All patients with malignant and nonmalignant diseases were hospitalised in the Lung Clinic of the Military Medical Academy, Belgrade, Yugoslavia, during the 12-month period from January to December 1989. Sera obtained from blood samples of 70 patients were stored at -20°C until use. Spicements of pleural effusion from 27 patients were obtained by thoracocentesis.

Serum and pleural–effusion TATI levels were determined by the immuno radiometric assay, using a commercial kit SPECTRIA TATI (Farmos Diagnostica, OULUNSALO, Finland). All measu-

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Table 1 – Distribution of malignant and nonmalignant lung diseases

Malignant:		Nonmalignant:	
bronchogenic carcinoma			
planocellular	15	tuberculosis	10
microcellular	13	bronchopneumonia and pleuropneumonia	5
adenocarcinoma	9	fibrosis	2
bronchoalveolar	3	sarcoidosis	2
nondiferentiated	11		
Total	51	Total	19

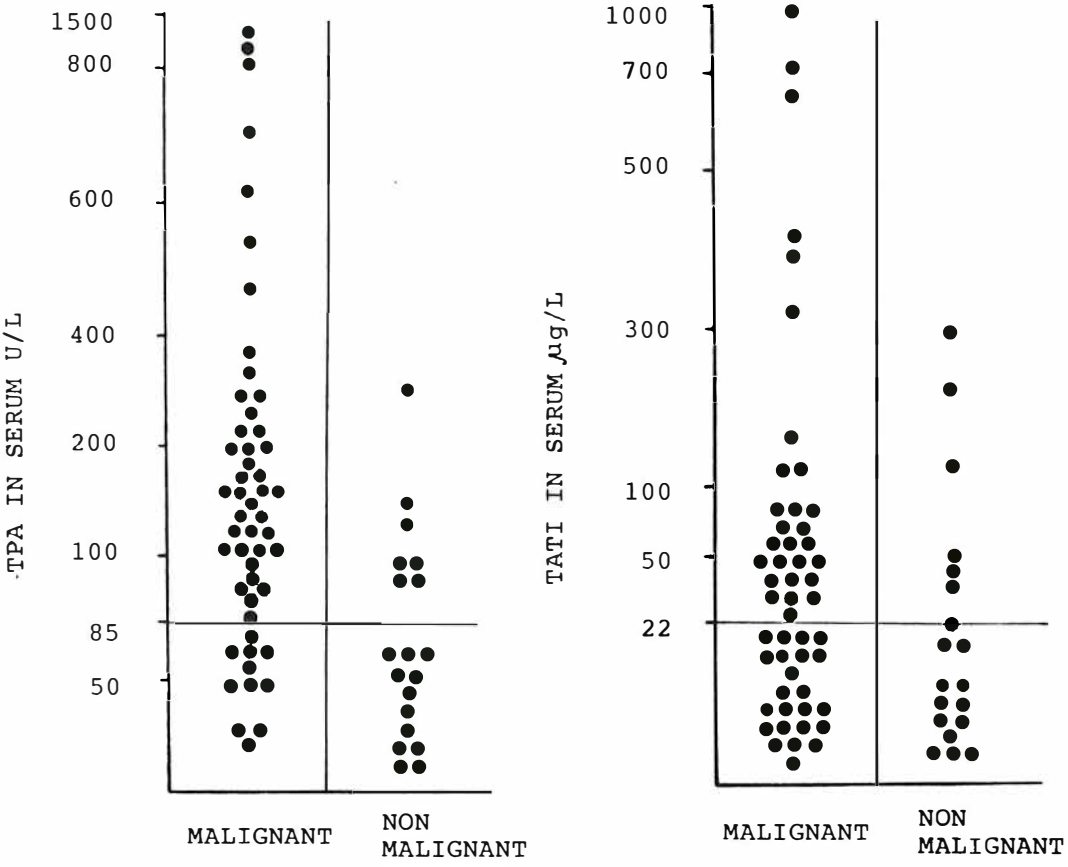

Fig. 1 – Concentration of TPA and TATI in serum of patients with malignant and nonmalignant lung diseases.

rements were performed in duplicate. The results were expressed in µg/L based on a reference standard. The results of measurements in 42 healthy subjects showed that the normal range of TATI was up to 22 µg/L. The intraassay and interaassay coefficients of variation (CV) were measured. The intraassay CV for TATI level was 8.1%. The interaassay CV from 11 assay performed with different lots of the kit was 9.3%.

Serum TPA level was measured in duplicate using the PROLIFIGEN^{R} TPA two–site immunoradiometric assay (IRMA). A commercial kit supplied by Sangtec Medical (Bromma, Sweden) with 85 U/L as the upper normal value was used.

Data were expressed statisticaly as the standard error of mean and were compared using Student's t test.

Results – Serum levels of TATI and TPA are presented in Figure 1. Apparently mean TATI concentration was higher in patients with malignant than in those with nonmalignant lung disease, but the difference was non significant ($p > 0.1$). Serum TPA concentrations were more elevated in patients with malignant than with non malignant diseases ($p < 0.01$).

Pleural effusion concentrations of TATI and TPA in patients with malignant and nonmalignant lung diseases are presented in Table 2.

Table 2 – Pleural effusion levels of TATI and TPA in patients with malignant and nonmalignant lung diseases

Group	n	TATI/μg/L±SE	TPA U/L±SE
malignant	13	72.7±48	4020.0±384
non–malignant	14	51.31±20	3091.5±427

Concentrations of TATI were not significantly different ($p = 0.347$). Serum levels of TPA were higher in patients with malignant than in those with nonmalignant diseases. Levels of TPA in pleural effusion were extremly high (it was about 10–fold higher), but difference between two groups (malignant and nonmalignant) were borderly nonsignificant ($p = 0.0590$).

As shown in table 3, the analysis of both markers regarding sensitivity, specificity and accuracy showed that TPA had better characteristics. TATI had satisfactory performance characteristics being higher that 50%. The best results in cancer detection were obtained by simmultaneous measurements of TATI and TPA.

Table 3 – Sensitivity, specificity and accuracy of two markers

	sensitivity (%)	specificity (%)	accuracy (%)
TATI	54.9	68.4	57.3
TPA	78.4	63.2	72.8

In our series 47 (92%) of 51 patients with malignant lung diseases had high TATI or TPA concentrations. Therefore, both markers reached normal range in four cases only.

Discussion – TATI and TPA have clearly shown their clinical usefulness as tumor markers in malignant pulmonary disease. Of 51 patients with malignant lung disease TATI levels were elevated in 27 (52.9%) and TPA in 42 (82.3%). Both TATI and TPA showed good sensitivity, but a rather low specificity (57% for TATI and 65% for TPA), which reflected that TATI and TPA concentrations were high, i.e. 43% and 35%, respectively.

No significant difference was found between serum and pleural effusion TATI concentrations in malignant or nonmalignant disease but pleural effusion concentration of TPA was higher than serum TPA concentration (4020.0 U/L versus 294.5 U/L in malignant and 3091.5 U/L versus 66-1 U/L in nonmalignant duseases). Our results differred from those reported by Larbre et al. (8) who found higher serum TATI levels in 35.5% patients with lung cancer. This difference may be due to the different stages of disease in comparable in both groups. As far as we know, pleural effusion TATI levels have not been reported TPA concentrations were in malignant effusion significantly higher than in nonmalignant effusion. It is non clear why TPA concentrations in effusion were more than 10-fold higher than in serum. Perhaps an inflammatory process in the pleura could be involved.

Conclusion – TATI and TPA seem to be good markers in pulmonary diseases, but neither of them showed sufficient sensitivity. The association of TATI with TPA allows greater precision in predicting the course of disease. In our series, 47 (92%) of 51 patients with malignant lung diseases had high TATI or TPA concentrations. Therefore, both markers reached normal range in four cases only. A combination of TATI with other serum markers, which are more specific for lung cancer as TPA, may be helpful in tumor detection and also contribute to better management of the patients throughout the course of disease. Concentrations of TATI is significantly higher in malignant than in nonmalignant diseases, but differences in the levels between serum and pleural effusions have been found. Pleural effusion TPA level were extremely high.

Sažetak

UPOREDNO ODREĐIVANJE TRIPSINSKOG INHIBITORA (TATI) I TKIVNOG POLIPEPTIDSKOG ANTIGENA (TPA) U SERUMU I PLEURALNOM IZLIVU U BOLESNIKA SA OBOLJENJIMA PLUĆA

Koncentracija tripsinskog inhibitora (TATI) merena je u serumu i pleuralnom izlivu u 70 bolesnika sa malignim i nemalignim oboljenjima pluća. Vrednosti koncentracije TATI upoređene su sa vrednostima TPA urađenim iz istog uzorka krvi. Merenje koncentracije TATI u serumu i pleuralnom izlivu izvedena je radioimunometrijskom metodom primenom tržišnog kompleta SPECTRIA TATI, firme Farmos Diagnostica. Nivo TPA određen je dvostranom radioimunometrijskom analizom primenom gotovog trzinskog kompleta PROLIFIGEN TPA firme Byk–Sangtec. Rezultati pokazuju da je koncentracija TATI i TPA u serumu značajno povećana u bolesnika sa malignim oboljenjima u odnosu na bolesnika sa ne malignim oboljenjima pluća. Koncentracija TATI u serumu i pleuralnom izlivu pokazuje visoku korelaciju, dok je koncentracija TPA u pleuralnom izlivu oko 10 puta veća u odnosu na koncentraciju u serumu. Osetljivost, specifičnost i tačnost zadovoljavaju za oba markera (TATI i TPA).

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THERAPY OF BILE DUCT TUMORS WITH A COMBINATION OF RESECTION AND INTRAARTERIAL INTRAHEPATIC CHEMOTHERAPY

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Abstract – Klatskin's tumors, (i.e. tumors of the upper third of the bile ducts) are rare. The survival of patients with operable and inoperable tumors is short. Considering that radical resections are often non feasibile and that microscopically evident residual disease is generally found even after presumably radical surgeries, such patients require an adjuvant chemotherapy or irradiation. Regional intraarterial chemotherapy and intraoperative irradiation have proved to be the most effective therapeutic methods. In our randomized clinical study, 8/23 patients with Klatskin's tumor after radical or nonradical surgery were treated by intraarterial intrahepatic chemotherapy (IAIHCT) with 5–Fluorouracil (5–FU) in the dose of 1000 mg/m^2. The mean observation period was 9 months (range 2-20 months). In the group of patients treated by chemotherapy 2 died 13 months after surgery on average. In the control group, 3 patients died directly after surgery, and another 3 on average 7 months after the procedure. The probability of 2–year survival in radically operated patients was 78% and in non–radically operated 40% ($p<0.1$), whereas in the patients treated by IAIHCT this probability was 72% regardless the radicality of previpus surgical treatment, in contrast to 42% calculated in the control group without IAIHCT $p<0.1$). Based on our preliminary results and the data from literature, we belive that intaarterial chemotherapy can prolong the survival of patients with this disease.

UDC: 616.361-006.6-08

Key words: bile duct neoplasms–therapy; survival

Orig sci paper

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Introduction – Malignant tumors of the bile ducts were first described by Fardel and Ciurvoisier by the end of the 19th century. The incidence of these malignomas in the world ranges between 2-10 patients per 100.000 population. Men are affeceted more frequently than women (1). According to the data of the Cancer Registry of Slovenia for 1986, 30 new cases of gale bladder and bile duct cancer were detected in men (incidence 3.1/100.000) and 91 in women (incidence 8.9/100.000) (2).

With regard to the site of their appearance, malignant tumors of the bile ducts are distributed as follows:
1) tumors of the upper third, known also as Klatskin's tumors, involving the left and the right hepatic duct in extrahepatic region, the hepatic bifurcation and the common hepatic duct; 2) tumors of the middle third (choledochus from the gall bladder orifice to the upper margin of the pancreas); 3) tumors of the lower third (intrapancreatic part of the choledochus) (3). Recent clinical studies indicate that the tumors of the upper third of the bile ducts are most frequent. As reported by Rossi et al. (4), there were 75% of Klatskin's tumors in their group of patients with bile duct tumors.

Pathohistologically, tumors of the bile ducts are distributed into 1) malignant epithelial tumors (adenocarcinoma, adenoacanthoma, adenosquamous and cholangiocarcinoma), and 2) less frequent malignant mesenchymal tumors (rhabdomyosarcoma, leiomyosarcoma, fibrous histiocytoma). The most forms are infiltrating–sclerosant and papillary adenocarcinomas. The latter are prognostically more favourable (1).

On the other hand, the prognosis of patients with Klatskin's tumors is still rather poor (5, 6, 7), despite the earlier diagnosis and more radical surgery. One–year and two–year survival of these patients after radical surgery is reported to be 45% and 25% respectively, whereas their five–year survival is only 1%. Any survivals exceeding the reported values are just a coincidence (1,8).

Despite the fact that tumors of the upper two thirds of the bile ducts rarely metastasize – namely, in only 1/3 the patients metastases in the liver, regional lymph nodes or other visceral organs can be found on surgery – a radical resection is often not feasibile owing to the adjoining portal vein, hepatic artery and liver parenchyme (7).

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Mizumoto et al. report that microscopic evidence of the disease can be found in 90% of patients after macropsocpically radical surgery (9).

Therefore, our randomized clinical study was aimed at establishing whether intraarterial intrahepatic chemotherapy could improve the survival and prognosis of patients with Klatskin's tumor.

Patients and methods – From June 1989 on, 23 patients with Klatskin's tumor have been entered into our prospective clinical study. The patients were randomized into a group with intraarterial intrahepatic chemotherapy (IAIHCT), and a control group. The group of treated patients comprised 12 females and 11 males in the mean age of 59 years (range 45-86 years).

Prior to surgery, all the patients presented with jaundice; mild hypoalbuminemia was evidenced in 4 and elevated body temperature in 1 patient. Four patients had liver metastases, 7 metastases in the regional lymph nodes, whereas 3 patients had both liver and regional lymph node metastases. Their mean performance status according to WHO was assessed as grade 2.

All 23 patients underwent surgery; this was assessed to have been radical in 9 patients, whereas skeletonization and atypical liver resection was performed in 3, skeletonization and graft implantation in 2, skeletonization and IV-B liver resection in 4, skeletonization and hepatectomy in 8, skeletonization alone in 1, bypass in 3, and explorative surgery with biopsy in 2 patients.

Postoperatively, 8 patients (3 with radical surgery) received 3 cycles of IAIHCT. The second group of 15 patients (6 with radical surgery) did not have postoperative chemotherapy.

Patient characteristrics are presented in Table 1.

The first course of postoperative IAIHCT with 1000 mg/m^2 was applied on days 1 and 2, 4-6 weeks after surgery; cycles were repeated every 4 weeks. Patients with radical surgery received 3 cycles and those with non–radical surgery 4 cycles of chemotherapy on average. After completed treatment, the patients were subject to regular follow up every 2 months. Radicality of surgery was assessed by means of surgical reports and pathohistological findings. Treatment success was evaluated according to the UICC criteria. The duration of survival and disease free survival were calculated from the day of surgery on.

Results – Of the total of 23 patients with Klatskin's tumor, 3 died on the 1st, 3rd and 17th postoperative day respectively. There are 15 patients still alive whereas 4 have been lost to follow up. The shortest observation period was 2 and the longest 20 months (mean 9 months).

Of 9 radically operated patients, 2 died 6 and 18 months respectively after surgery. Their mean duration of survival was 12 months. Three of these patients received adjuvant IAIHCT. All of them are without evidence of disease (NED) 6, 11 and 16 months respecitively (mean 11 months).

Of 14 non–radically operated patients, 5 received IAIHCT; 2 of them died 12 and 14 months respectively after surgery. Of 9 deceased patients, 3 died immediately after surgery whereas one patient died 2 months after the procedure. The probability of 2–year survival following radical surgery is 72% and after non–radical surgery 40% ($p<0.1$) (Fig. 1).

The probability of 2–year survival in patients with Klatskin's tumor postoperatively treated by IAIHCT is 72% regardless the radicality of treatment, whereas the survival rate in those without IAIHCT is expected to be only 47% ($p < 0.1$) (Fig. 2).

The disease–free survival of patients with Klatskin's tumor after radical surgery was the following:

Patients with IAIHCT (3/9) survived 6, 11 and 16 months respectively (mean 11 months).

Patients without IAIHCT (6/9) survived 4 and 6 months (mean 5 months).

The disease–free survival of patients with Klatskin's tumor after non–radical surgery was the following:

Patients with IAIHCT (5/11) survived 5, 6, 7, 7 and 12 months respectively (mean 7 months).

Patients without IAIHCT (6/11): of the 2 evaluable patients, one is without evidence of disease 2 months after surgery.

Side effects : Of 23 patients, 3 died immediately after surgery. Postoperatively, one patient presented with pathological liver test findings, one had bilateral fistulae and another one a subphrenic abscess. In 16 patients postoperative course was uneventful.

Of altogether 31 IAIHCT–related complications, gastritis was observed in 2 patients, hemorrhagic gastritis in 1, chemically induced hepatitis in 1, vascular spasm on celliacography in 1 and upper abdominal pain following celliacography in 3 patients. All these adverse reactions were of transient nature.

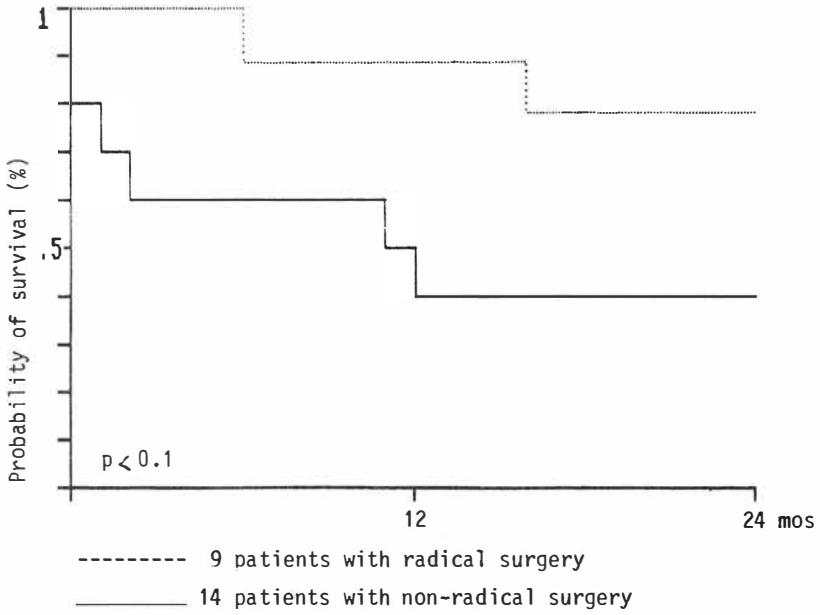

Fig. 1 – Survival of patients with Klatskin's tumor after radical and non-radical surgery

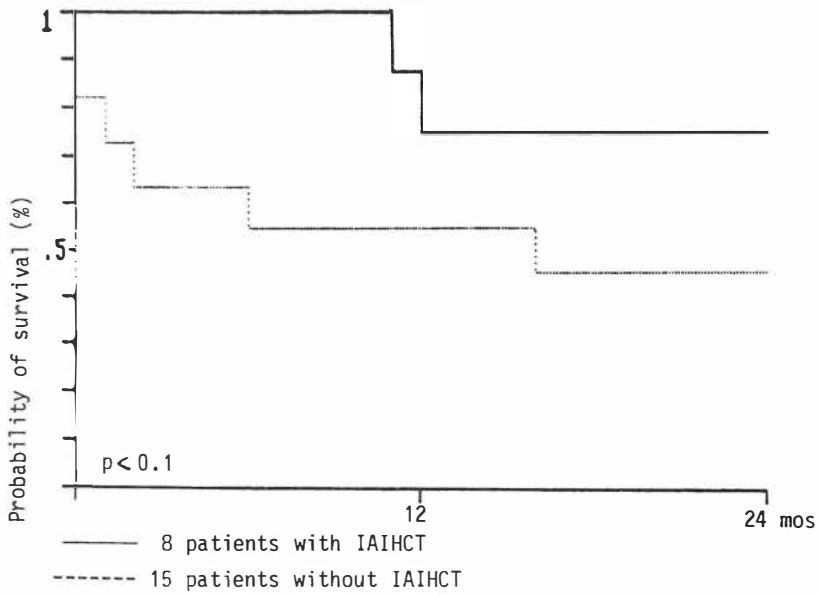

Fig. 2 – Survival of patients with Klatskin's tumor with or without IAIHCT

Discussion – So far, the role of radiotherapy in the treatment of bile duct tumors has not been clearly defined. The results of a retrospective study on the use of percutaneous irradiation with 24000–5000 cGy indicate that 6–month survival achieved in non–irradiated patients could be prolonged to 19 months in the irradiated group (10). Fogel reports on 11 month mean survival and 6% 5-year survival achieved in a group of 35 nonresectable irradiated patients (11). Nowadays many authors believe that in locally advanced tumors a curative dose of percutaneous irradiation ranges between 6000 – 7000 cGy delivered in 6 to 8 weeks. With microscopically evident residual disease after resection, however, a dose between 4500 – 5000 cGy is recommended (1, 12, 13). Nevertheless, in percutaneous irradiation a tumoricidal dose is difficult to achieve, despite the small irradiation fields, owing to the risk of damage to the surrounding tissue. This can be avoided by using brachytherapy and a lower cumulative dose of percutaneous irradiation (13).

As to the intraoperative irradiation of nonresectable tumors with a single dose of 3000 cGy, this method is reported to have resulted in recanalization of obstructed bile ducts and a prolonged survival. Abe and Takahashi (12) claimed such an effect, i.e. recanalization of obstructed bile ducts, being achieved in 90% od 59 patients treated by intraoperative irradiation with a single dose of 2500–4000 cGy. The patient tolerated the treatment well. The analysis of autopsied patients revealed that a single dose of 3500 cGy could be regarded as potentially curative.

Low incidence and frequent occurrence of liver damage or hiperbillirubinemia often render the treatment with cytotoxic agents unfeasible, and therefore only few patients with tumors of the bile ducts are treated by chemotherapy. According to the results of some more relevant clinical studies, a short-lasting partial response can be achieved in only 1/4 of these patients (Table 2).

In tumors of the bile ducts a systemic polychemotherapy according to the FAM schedule (5–FU, Doxorubicine, Mitomycin–C) is still believed to be the most effective (19). Thought the results of many studies indicate that systemic chemotherapy may prolong the survival of patients for 6–11 months on average, the real value of this

Table 2 – Systemic chemotherapy for bile duct cancer

Drug	No. of patients	Partial No.	Response (%)
5-FU (14)	17	4	(24)
Mitomycin C (14)	15	7	(47)
FAM (15)	14	4	(29)
FAM (16)	13	4	(31)
5-FU (17)	12	1	(8)
5-FU + MeCCNU (17)	12	2	(17)
Ftorafur + adriamycin + BCNU (18)	7	3	(43)
Total	90	25	(26)

5-FU = 5-fluorouracil, FAM = 5-FU + adriamycin + mitomycin C, MeCCNU= 1-(2-chlorethyl)-3(4-methyl-cyclohexyl)-1-nitrosourea, BCNU = 1.3-bis (2-chloroethyl)-3-cyclohexyl-1-nitrosourea.

Table 1 – Characteristics of patients with Klatskin's tumor

Primary tumor site	No. of pts	Radical surgery	Nonradical surgery	IAIHCT after non-radical surgery	Adjuvant IAIHCT	Regional metastases
Common bile duct B-1	4	3	1	0	2	0
Confluence II	6	3	3	1	0	4
L. hepatic duct III b	9	3	6	3	1	5
R. hepatic duct III a	1	0	1	1	0	0
Central hepatic duct – IV	3	0	3	0	0	3
Total	25	9	14	5	3	11

IAIHCT – intraarterial intrahepatic chemotherapy

treatment is questionable, taking into account the lowered quality of life and chemotherapy–related side effects.

A majority of patients with bile duct cancer die of locoregional disease and not because of distant metastases. Considering negligible effects of systemic chemotherapy and hardly feasible intraoperative irradiation, as well as a small tumor volume, the regional or intraarterial chemotherapy is frequently believed to be the treatment of choice.

In the last 20 years there were many reports published on the use of chemotherapy in patients with primary tumors of the liver or hepatic metastases, particularly those originating from colorectal cancer. A majority of authors claim that intraarterial chemotherapy by means of a percutaneous or surgically inserted catheter has the potential of increasing the rate of objective responses, prolonging the survival and improving the quality of patient's life (20, 21).

Unfortunately, during all these years there has been only one randomized clinical study carried out where a group of untreated patients was compared with a group treated by intraarterial chemotherapy. According to the obtained results, patients in the latter group survived 375 days whereas the survival in the untreated controls was only 55 days. However, in the control group there were also some patients who did not meet the requirements for i.a. therapy (22). Apart from the above, no other such randomized clinical study comparing the results of i.a. therapy with systemic treatment or untreated patients has been performed so far. Therefore, also the supposition that i.a. ChT may prolong the survival is not based on reliable evidence. The encouraging results (approximately 50% of objective responses) could be due to patient selection. Namely, such clinical studies generally comprise patients in good general condition which permits for surgery or percutaneous insertion of catheters and chemotherapy. These patients do not have distant metastases, and present with satisfactory hepatic function; they are also free of hypoproteinemia, jaundice and ascites. These prognostic factors alone may indicate that the patient has 50% chances of surviving one year (1).

The number of patients with tumors of the upper two thirds of the bile ducts, treated by i.a. chemotherapy and included in a randomized clinical study is 2 – 15. The small number of patients as well as the scarcity of such studies render a reliable assessment of the true value of i.a. chemotherapy difficult.

Warren et al. (23) report on a group of 41 patients with non–resectable tumors of the bile ducts, 15 of which received i.a.. chemotherapy with FUDR. Sixteen of these patients survived longer than 1 year. Of these, 9 (60%) were treated by i.a. chemotherapy. One patient survived over 3 years.

In other three studies (24, 25, 26) where 8, 11, and 10 patients respectively were treated with FUDR (floxuridine), the rate of objective responses (partial responses) ranged between 20–50%.

As reported by Smith et al. (27), two partial responses were achieved in 4 patients treated with i.a. applications of Mitomycin–C and 5–FU, whereas Garnick et al. (28) and Messney et al. report on one partial remission achieved in 2 patients treated with doxorubycin, and 32 patients receiving 5–FU respectively.

The number of IAIHCT treated patients with Klatskin's tumor included in our study is relatively small, and the observation period is short as well. At that, 3 patients received adjuvant IAIHCT.

Despite the longer survival observed in the treated patients, the efficacy of such therapy cannot be statistically confirmed.

5–FU is metabolically processed in the liver, and afterwards excreted through the bile ducts. A high concentration of medication in the bile ducts and liver probably has a very positive effect on the remaining tumorous tissue. On the first passage of medication through the liver a part of the substance undergoes detoxification. This may explain why, despite its higher regional concentration of the drug, the presented treatment entails less side effects than systemic therapy.

Regional toxicity of i.a. chemotherapy, however, is associated with severe problems. Among these, drug–induced sclerosant cholangitis, increased aminotransferases, toxic hepatitis, biliary stasis, focal necroses of the liver and chemical cholecystitis are observed most frequently. According to the report by Hohn et al. (30), in a group of 55 patients treated with FUDR, drug–induced sclerosant cholangitis was observed in 56%, chemical cholecystitis in 9%, and increased aminotransferase immediately after completed treatment in 96% of the patients. In our group a transitional increase in aminotransferase levels immediately after 5–FU application was noted in only 30% of patients. None of them presented with sclerosant cholangitis. There were no treatment–related deaths.

Conclusion – The existing experience with regional chemotherapy in patients with Klatskin's tumor is still scarce. Frequent, microscopically evident nonradical surgeries and poor prognosis of the patients render an adjuvant treatment necessary. When comparing the regional chemotherapy with the systemic one, the former approach has the following advantages: lesser side effects, short hospitalization period, and a better quality of life. Based on our experience, we believe that the regional chemotherapy has the potential of improving the prognosis in patients with Klatskin's tumor.

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MONOCLONAL ANTIBODIES IN THE TREATMENT OF BREAST CARCINOMA

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Abstract – In order to find specific reagents for the diagnosis and treatment of breast carcinoma numerous monoclonal antibodies have been produced. This review deals with the trials involving monoclonal antibodies for breast carcinoma treatment: radiolabeled monoclonal antibodies, immunotoxins, chemoimmunoconjugates and monoclonal antibodies used alone. The major obstacles to cancer therapy are discussed: the lack of specificity of monoclonal antibodies, heterogeneity and modulation of tumor antigens, and human anti-mouse immunological response. The possibilities to circumvent this obstacles are indicated: the use of the combination of monoclonal antibodies; human, chimeric and antiidiotypic antibodies; antibody fragments instead of the whole immunoglobulin molecule etc.

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Key words: breast neoplasms-therapy; antibodies, monoclonal

Review paper

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Introduction – Carcinoma of the breast is the most common malignant disease in women and the leading cause of mortality among western women (1,2). Numerous investigations are aimed today to find new possibilities of breast carcinoma treatment. Monoclonal antibodies which bind to specific antigens, represent one of these possibilities.

In 1975, Kohler and Milstein made the seminal report of production of monoclonal antibodies by using method of cell hybridisation, for which they received the Nobel Prize (3). Cultures of myeloma cells can be fused to lymphocytes from immunised animals to form hybrid cells that grow continously in culture and secrete antibodies specific for the antigen against which the animal was immunised. This technology has made it possible to generate high affinity antibodies of a required specifity and in limitless quantities (4, 5). Since then, this principle has been used for the production of numerous monoclonal antibodies to breast carcinoma antigens, and there are attempts to use some of them for the treatment of this disease (6-9).

Discussion – Monoclonal antibodies have been studied for their effect on cells grown in culture (10, 11), on human carcinomas of the breast grafted in experimental animals (12, 13), and also, monoclonal antibodies have been directly applied in some patients with breast carcinoma. This was particularly the case when other modalities of treatment were relatively ineffective (9, 14, 15). Monoclonal antibodies can kill tumor cells by several mechanisms, depending on whether they are applied alone, or conjugated with different cytotoxic substances such as radioisotopes, toxines, chemotherapeutic agents, etc. If monoclonal antibodies are applied alone, they can kill tumor cells indirectly by complement-dependent cytotoxicity or cell mediated cytotoxicity (2). Growth of human carcinoma of the breast grafted into nude mice can be reduced by more than 80 per cent if a combination of monoclonal antibodies produced to human milk fat globule membranes is given to the mouse prior to tumor implantation. The reduction in growth in less than 50 per cent if the antibodies are administered after implantation (16, 17). According some other authors, passive immunotherapy with monoclonal antibodies used alone can not be succesful, because the cellular immunity plays the main role in the natural immunological defense against tumor (18, 19). There are seve-

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ral reports of trails in which monoclonal antibodies impaired the proliferation of tumor cells by inhibiting growth factors or otherwise by altering the regulation of the target cells. So, monoclonal antibodies directed against receptors for transferrin (20, 21), for interleukin-2(22, 23) and for epidermal growth factor (24, 25) could compete with the growth factors and impair the proliferative capacity of tumor cells. This way of immunotherapy seems to be more effective in leukaemias (22, 26).

The basis of the therapeutic application of conjugated monoclonal antibodies is the linking of monoclonal antibodies with radioisotopes, natural toxines, chemotherapeutical agents or with other substances which modify immunological response. Such »immunoconjugates« could kill tumor cells *in vivo* because of their selective toxicity. In mice with human breast carcinoma xenografts, monoclonal antibodies to human milk fat globule membranes (HMFGM 1 and HMFGM 2), conjugated with iodine 125, reduced the size of tumors by 60 per cent (2, 30). Monoclonal antibodies to human milk fat globule membranes were also conjugated with iodine 131 and injected to the patients intracavitary, on the place from which breast aspiration with malignant cells was taken. After this treatment, by repeated breast aspirations, malignant cells were not found (31, 32). By the systemic injecting of radioiodinated monoclonal antibodies it was possible to destroy the epithelial cells of human breast tumors implanted in nude mice (33). Relatively greater success with regional application of monoclonal antibodies could be explained by cross-reactivity with normal tissue antigens and by poor access and penetration into the tumor by systemic therapeutic application of monoclonal antibodies (9).

Among toxins, the most commonly used for the conjugation with monoclonal antibodies is the A-chain of the plant toxin, ricin (34-36). *In vitro* and *in vivo,* many tumor cells have been destroyed in this way (37, 38), but 20–30% per cent of tumor cells remain viable, what is probably the reflection of the heterogeneity of tumor cells (14).

Different chemotherapeutic agents can also be used for the conjugation with monoclonal antibodies, and they form so called chemoimmunoconjugates (39). Investigators have explored conjugation of various agents, including anthracyclines such as daunorubicin (40-42), alkylating agents such as chlorambucil (43), and also antimetabolites such as methotrexate (44-46). Chemoimmunoconjugates have been studied for their effect mainly on tumor cells grown in culture, or on experimental animals, but there are only few attempts of direct application to the patients (47, 48).

There are numerous factors which make the application of monoclonal antibodies in the breast carcinoma treatment rather complicated. Two major obstacles are: pronounced heterogeneity and modulation of tumor antigens, and the lack of absolute specifity of monoclonal antibodies (1,8,9). Tumor cells exhibit pronounced heterogeneity, so even in the same tumor cells differ as to their phenotypic and in genotypic characteristics (49). It could be the result of different cell subpopulations from which the tumor originates, of the modulation or loss of the antigens of tumor cells, and finally, heterogeneity could also occur because the tumor cells were in different stages of differentiation, or in different stages of the cell cycle (50-53). Tumor cells are also genetically very instable. Constant genomic changes and selective pressure of their inviroment (immunological system or given therapy) result in heterogeneity of the tumor cells (53). It is belived that this problem could be partly overcome by conjugation of monoclonal antibodies with isotopes. The effect of radiation is carried over five cell diameters, so that not all tumor cells need to possess the antigen to be destroyed (2). To date, many monoclonal antibodies produced to breast carcinoma antigens have been described, but none of them is specific only for breast carcinoma. They mostly also react with normal tissues and/or with other tumors, although generally to a much lesser degree than with breast cancer (1). But, the therapeutic application of several monoclonal antibodies in combination at the same time, has an undoubted clinical value (7,9,54,55).

One of important limitations associated with the application of monoclonal antibodies includes the development of human antimouse antibody response. Human antimouse antibodies are formed after the repeated doses of murine monoclonal antibodies. They can be directed towards the isotype of a constant region or towards the idiotype of a variabile region of murine immunoglobulines (56). These antibodies can inhibit the effect of primarily given mouse monoclonal antibodies (57), and also they can couse in some patients allergic reactions, such as serum sickness, renal toxicity and various adverse reactions (56,57). Some clinical trials have led to the suggestion that an immune response against the murine immunoglobulins could be beneficial, be-

cause these secondary antibodies could additionaly induce an immune attack by the host against the tumor antigens (58, 59). There are some attempts of therapy whith antiidiotypic antibodies (60–62).

The development of human immunological response to murine monoclonal antibodies is avoided by the therapeutic application of human monoclonal antibodies (63-66). But, great growth instability, tendency of loosing chromosomes, and weak production of monoclonal antobodies are the characteristics of human hybridomas (67). Genetic engineering technologies have made it possible to make chimeric monoclonal antibodies (human heavy chaines and murine light chaines of immunoglobulin molecules), which are much less immunogenic (68, 69). Reports about very few clinical investigations have been published (70, 71). Because of the immunogenicity problems caused by the Fc portion of the murine immunoglobulin molecule, there are some attempts of therapy with antibody fragments-Fab or $F(ab')_2$, where Fc portion is removed (72). Molecules, like toxines or chemotherapeutic agents, conjugated to these fragments, penetrate much easier to tumor interstitium (73), but rapid clearing in the kidney greatly impairs the ability to concentrate the reagent in the tumor (10).

Conclusion – The application of monoclonal antibodies in the treatment of malignances in general, and also in the treatment of breast carcinoma, still represents a great challange for many investigators. There are more successful results *in vitro* and in animal models, but examples of direct clinical application are still insufficient. Obviously, more time is required to proove the real value of such therapeutic approach to the treatment of breast carcinoma. The progress which has been already made is the reason for the optimistic point of view.

Sažetak

PRIMJENA MONOKLONSKIH PROTUTIJELA U TERAPIJI KARCINOMA DOJKE

U cilju pronalaženja specifičnih supstanci za dijagnostiku i terapiju karcinoma dojke, do danas su proizvedena brojna monoklonska protutijela. U ovom preglednom članku prikazani su pokušaji primjene monoklonskih protutijela u terapiji karcinoma dojke: primjena monoklonskih protutijela vezanih na radioaktivne elemente, citostatike, ili toksine, kao i primjena samih monoklonskih protutijela. Navedene su i osnovne zapreke u terapijskoj primjeni monoklonskih protutijela: heterogenost tumorskih antigena, nedostatak apsolutne specifičnosti monoklonskih protutijela, kao i imunološki odgovor pacijenata na unos mišjih imunoglobulina. Naznačene su i mogućnosti prevladavanja ovih poteškoća: terapijska primjena kombinacije monoklonskih protutijela; humana, himerična, te antitidiotipska antitijela; primjena fragmenata antitijela umjesto cijele molekule imunoglobulina itd.

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FROM PRACTICE TO PRACTICE
Case 3

Answer: This is an Intra–arterial digital subtraction (DSA) aortogram which shows that there is occlusion of the left renal artery and a severe stenosis of the right renal artery. In addition, although the hepatic and splenic arteries are fairly well opacified there is hardly any opacification of the branches of the superior mesenteric artery (SMA), suggesting that there is significant stenosis of the origin of the SMA. This could be confirmed by a lateral aortogram, which will show stenosis or occlusion of the SMA. There is also a linear subtraction artefact to the right of the lumen of the aorta, which is caused by movement of the calcified aortic wall, indicating that there is extensive disease of the aortic wall.

This patient has a severe renal artery stenosis affecting his only kidney. Although there is debate about the role of other imaging studies (e.e. isotope studies) in selecting patients for renal artery angioplasty, in this situation the patient has a high risk of infarcting his remaining kidney and further imaging of the kidneys is redundant as there is no doubt that the stenosis needs treatment. In this situation angioplasty, with readily available surgical back–up and suitable angioplasty experience, is often the treatment of choice. In this patient the angioplasty was successful in relieving hypertension and improving renal function (Fig. 1b).

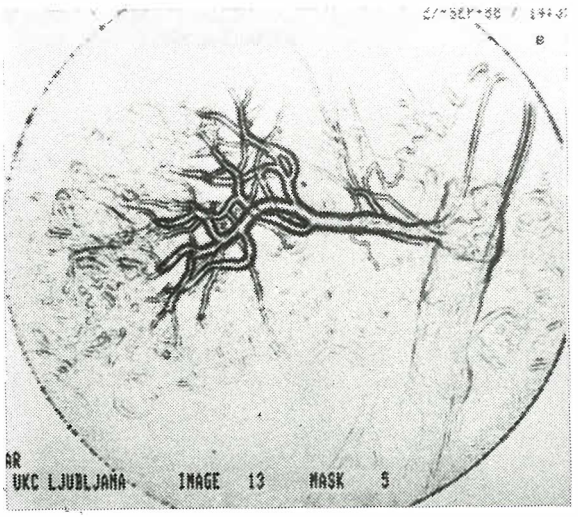

Fig. 1b – The post–angioplasty angiogram

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UNIVERZITET U SARAJEVU, PRIRODNO–MATEMATIČKI FAKULTET, ODSJEK ZA HEMIJU

SOME APPLICATIONS OF NONDESTRUCTIVE RADIOACTIVATION ANALYSIS IN MEDICINE

Zovko E

Abstract – The elimination of gold in form of ^{198}Au radioisotope from the organism of a patient with rheumatic fever to whom myochrisine (di-natrium salt of aurithiomaleic acid) had been applied intramuscularly, was followed by means of radioactivated analysis.
The application of gold preparations, due to possible disturbances, especially in the kidney function, requires the monitoring of gold content in urine, which was done in the first phase of the programme.
In the second phase of the programme, gold from the radiated sample was separated, i.e. gold was extracted with mercury, in order to avoid disturbances from other nuclides in traces (Ag, Rb, Fe, Co, Zn) which are also present in the patient's urine.
We can conclude from the curve of the elimination of gold by kidney function that elimination of gold by means of urine, after intramuscular injection of myochrisine, is a relatively slow process.

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Key words: rheumatic fever-drug therapy; metabolic clearance rate: gold Radioisotopes

Orig sci paper

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Introduction – In some cases of rheumatic arthritis, patients are treated with intramuscular injections of a preparation of gold called myochrisine (di-natrium salt of aurithiomaleic acid).

Since clinical practice requires following of the preparations of gold, the aim was to monitor the quantity of gold in patient's urine by means of the nondestructive radio activation analysis, and to test the possibility of extracting isotope ^{198}Au from the mixture after neutron radiation (1,2).

Based on the obtained data, the approximate quantity of gold eliminated from patient's organism through urine was estimated after an intramuscular injection of 50 mg of myochrisine (3).

Material and methods – Urine of a patients with rheumatic arthritis was used as a sample.

In the first phase of the programme, the whole dry residue of urine was radiated at the Institute »Boris Kidrič« in Vinča, in order to determine the complex urine spectrum and other radionuclides which are likely to be found in urine (Fig. 1).

In the second phase of the programme, new series of samples were prepared for the quantitative determination of gold in urine, using created isotope ^{198}Au.

Samples of urine (10 ml), with ampullated gold standard ($1.2\ 10^{-6}$ g) were placed into the common channel of the reactor ($1,5\ 10^{13}$ n/sec cm^2) and the comparison of yield of isotope ^{198} Au against the standard was done by means of comparative method of radioactivted analysis.

Due to the possibility of disturbance of some other nuclides, in the latter phase of the programme, a simple radiochemical procedure for the separation of gold from the radiated sample was developed.

The extraction of gold by means of elementary mercury was applied (4).

Measurment of the radiated samples was performed on a 4096 Ge-Li detector at the Institute »Boris Kidrič« in Vinča and on multichannel γ spectrometer with NaJ/T1/, at this Institute.

The purpose of these parallel measurments was to estimate whether both systems are equally worth using for determination of ^{198} Au in urine.

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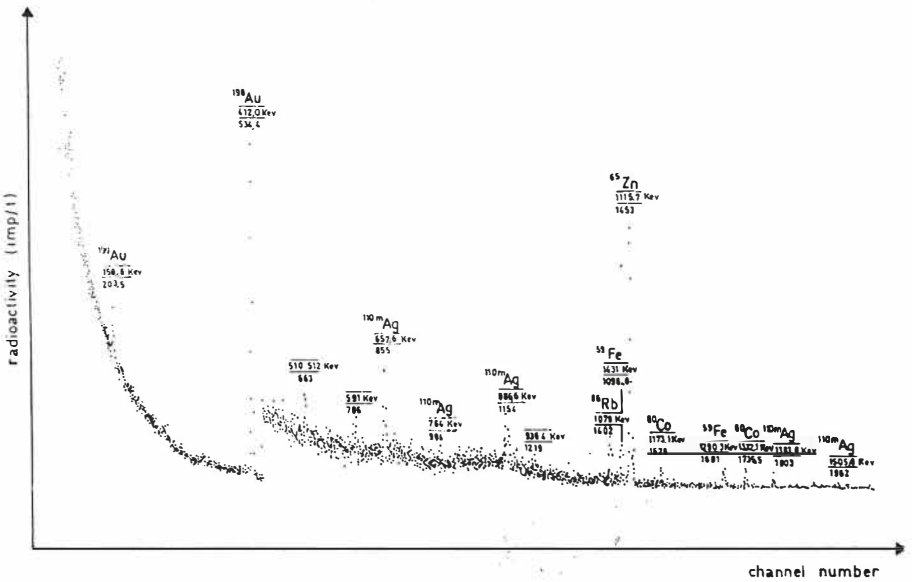

Fig. 1 – γ spectrum of urine

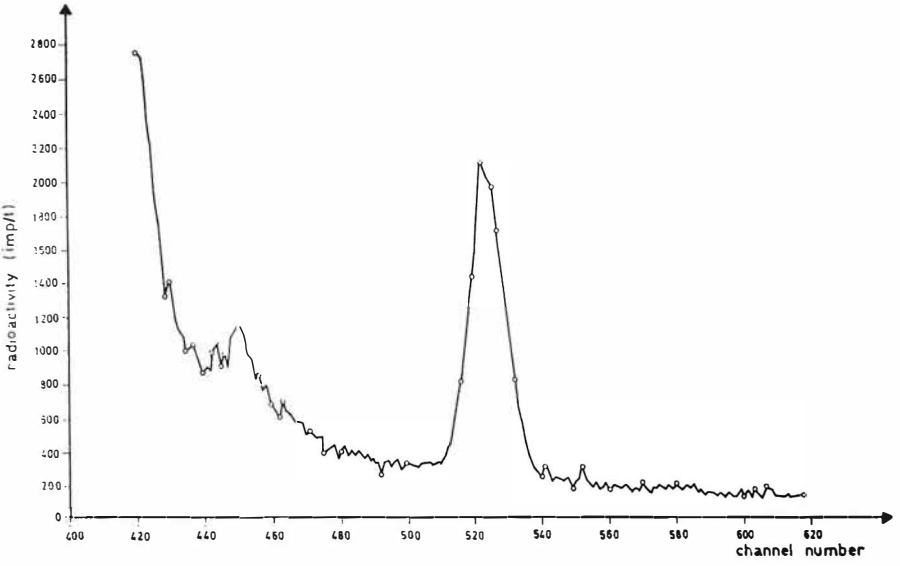

Fig. 2 – γ spectrum of ^{198}Au extracted from urine

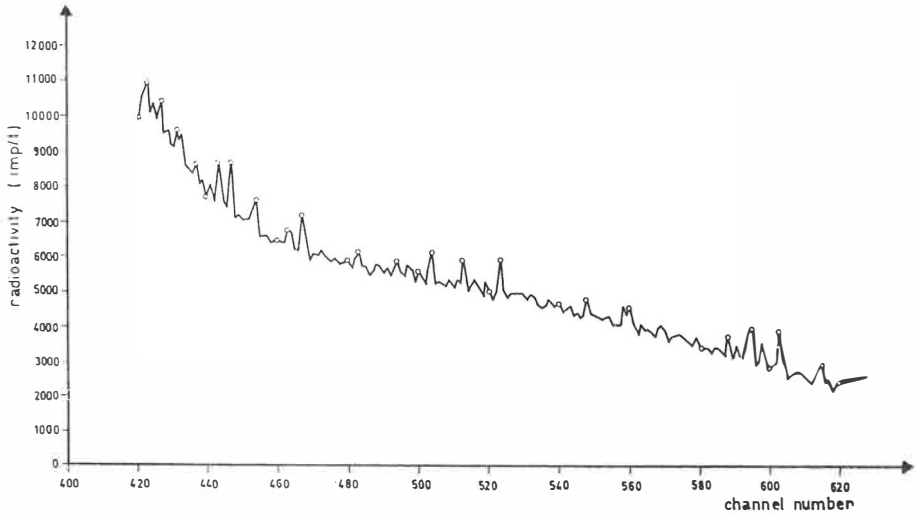

Fig. 3 – γ spectrum of other nuclides present in the urine

Table 1

Urine	Test number	Measured in Vinča (Ge-Li) mg/2000 ml	Measured in Sarajevo NaJ (1) mg/2000 ml	Measured on NaJ (T1) after extrac. I	II	III	Amid. for extrac.
1st day	1	1.85	1.80	1.69	1.68	1.69	1.68
2nd day	2	1.55	1.43	1.37	1.28	1.31	1.32
3rd day	3	0.88	0.88	0.87	0.87	0.88	0.87
4th day	4	1.25	1.23	1.45	1.36	1.40	1.40
5th day	5	0.93	0.93	0.68	0.70	0.67	0.68

Results – We have presented:

γ spectrum of ^{198} Au extracted from urine (Fig. 2)

γ spectrum of other nuclides in urine (Fig. 3)

On the basis of the results of series of radiated samples, comparative table for all analyses of that series of radiated samples is given hereunder (Table 1), with the survey of gold elimination by means of urine in a patient on gold therapy (Fig. 4).

Discussion – The quantity of electrolite and the content of various reductive organic materials in urine vary from case to case, so we should expect gold to appear both in its ionic and elementary forms, in a different degree of colloidal dispersity.

All these reasons make the process of gold determination in urine rather unreliable, regardless the method applied, so we decided to choose a very delicate and reliable method of radioactivation analysis (5, 6).

Since the presence of other elements in urine partly complicates the simple γ spectrometric procedure of ^{198} Au determination the possibility of separation of ^{198} Au from other isotopes by extraction of gold with elementary mercury was examined.

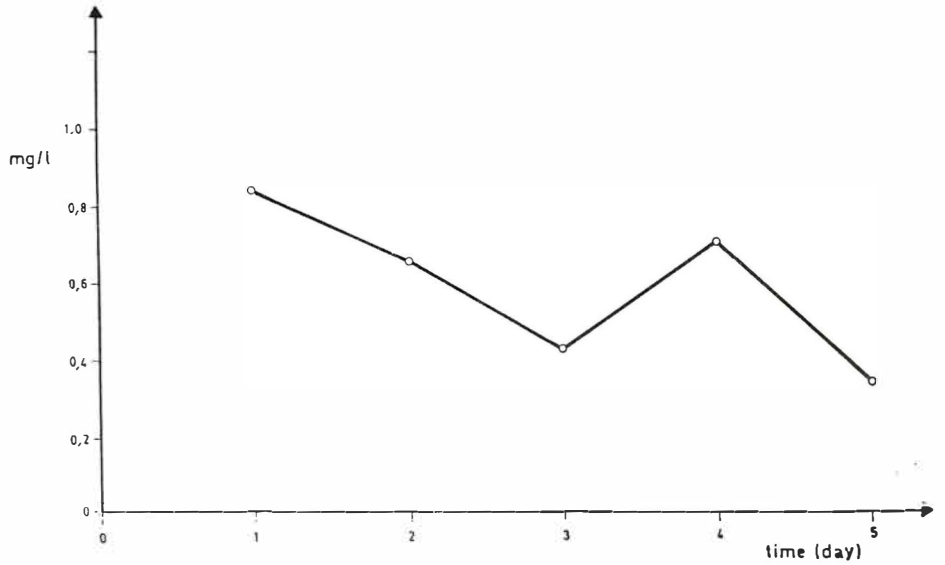

Fig. 4 – Levels of ^{198}Au in urine at various times

Conclusion – After the intramuscular injection of 50 ml of mychrosine (di-natrium salt of aurithiomaleic acid), in the first five days, with average urinary function of kidneys, the patient excreted about 6 mg of gold.

We can conclude from the curve showing the elimination of gold by kidney function that the elimination of gold is relatively slow process.

Since the measurment of radiated samples is performed both on a 4098 Ge-Li and a multichannel NaJ/T1/ detector, by processing the data for photo-peaks of standards and samples of ^{198} Au, high coincidence of different measuring techniques is obtained.

Sažetak

NEKE PRIMJENE NEDESTRUKTIVNE RADIOAKTIVACIONE ANALIZE U MEDICINI

Praćena je eliminacija zlata – kao radioizotopa ^{198}Au – iz organizma oboljelog od reumatične groznice, kome je prethodno i/m apliciran myochrisin (dinatrijumova so aurotiojabučne kiseline), nedestruktivnom radioaktivacionom analizom.

Primjena preparata zlata, radi mogućih smetnji posebno na funkciju bubrega, traži da se prati sadržaj zlata u urinu, što je i učinjeno u prvoj fazi programa.

U drugoj fazi programa se pristupilo separaciji zlata od ozračenog uzorka, tj. ekstrakciji zlata sa živom, da bi se izbjegle smetnje drugih nuklida u tragovima (Ag, Rb, Fe, Co, Zn), koji se također nalaze u urinu oboljelog.

Iz toka krive eliminacije zlata funkcijom bubrega, može se zaključiti da je odbacivanje zlata urinom, nakon intramuskularne injekcije myochrisinom, relativno spor proces.

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SCINTIGRAPHIC FILM SENSITOMETRY AND IMAGE QUALITY ASSURANCE IN NUCLEAR MEDICINE USING MICROSCOPE

Kasal B

Abstract – The sensitivity of the film and its corresponding characteristic curves are usually determined by exposing a step wedge to the flashes of light of standard color temperature and developing the film under well defined and carefully controlled processing conditions. Radiographic films are also tested by exposing a plastic step wedge to the penetrating X–rays in fixed and standard way. For densitometric readings a high cost densitometer is used. So obtained characteristic curves, unfortunately, are not relevant enough to be used in nuclear medicine where the images are formed by recording certain count density distributions from the CRT of a multiformat imager. The step wedge exposure source should relate to the film use in order the sensitometric results be meaningful.

In this work the automatic exposure control unit of our cytological microscope was used for indirect determination of optical densities. Excellent correlation between the high quality densitometer readings and exposure timer for cytologic photography was obtained.

Sets of flood images recorded within the wide range of count densities were analysed and high quality film characteristic curves giving the relationship of optical density vs. logarithm of the count density were produced. Different parameters which could influence the shape of the curve as well as the film speed are mentioned and the necessity of some kind of standardization is discussed.

UDC: 539.163.08

Key words: radionuclide imaging; x–ray film; densitorentny, microscopy

Orig sci paper

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Introduction – If the densities obtained in a photographic emulsion are plotted against the logarithm of the exposures to which the emulsion has been exposed, the resulting curve is designated as an H and D curve, after Hurter and Driffield (1) who first used it to characterize photographic emulsions. This «characteristic curve» is very sensitive to different physical factors (2, 3, 4) and every change is immeditely reflected in diagnostic image quality (5, 6).

Films to be used in nuclear medicine image multiformaters, like the Microdot used in this work, have to be sensitive to the blue light flashes with peak intensity at 425 nm produced by the oscilloscope phosphor of the P11 type and this is the case with our film (7). Other phosphor types will change the characteristic H and D curve of the film.

A static scintigraphic image is typically formed by recording several hundreds of thousands of light flashes randomly distributed over a period of few minutes. The superposition of dots is not excluded. Such particularities, when compared to usal simple exposures, limit the importance of a typical J and D curve for nuclear medicine applications. It is much more appropriate to produce the curves where optical densities of the images of a uniform flood surce are plotted against logarithms of the mean count densities, but this is usually not done.

Optical densities in film industry are usually measured with high quality (and price) transmission densitometers. In this work it is shown how a laboratory microscope equipped with a photomicrographic unit can well be used for the same purpose.

Material and methods – Optical density of a photographic film is defined as a logarithm of the ratio of incedent to transmitted light, which means that the density is independent of the quality and the intensity of the light used for densitometry.

The step wedge Fig.1 recorded on Fotokemika FNM film for nuclear medicine was analysed using a high precision transmission densitometer of Macbeth type assigning an optical density value D_i to each blackenning of the step wedge. This set or readings was taken as reference for later correlation with the microscope results.

A single exposure of a standard step wedge in standard conditions [controlled color temperature (2660°K) and intensity of light (illumination = 200 Lux), fixed time and temperature of film

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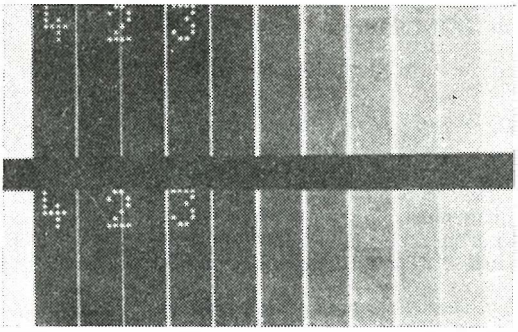

Fig. 1 – A typical step wedge used for calibration of the microscope–exposure unit system. Some of the steps are not visible because of the limited capabilities of the photographic paper when compared to the film.

development (FR = 90 S, 90 sec, 34°C)] is completely adequate to producing a step wedge by exposing a film to the light of fixed intensity and other above mentioned conditions, but for different exposure times. Photographic exposure of the i–th step E_i is a produced of the exposure light intensity I_E and the exposure time t_{Ei} x On X–axis of a H and D curve we have logarithms of exposures E_i corresponding to optical densities D_i read by the transmission densitometer. Namely,

$$\log E_i = \log (I_E \times t_{Ei}) = C_E + \log t_{Ei} \quad [1]$$

where C_E is a constant.

In the Department there is an Olympus microscope of the BH–2 series fitted with the photomicrographic system MP–0 ADS including an automatic exposure control unit. The whole system is used for analysing and photographing cytological samples. Taking into account the sensitivity of the film to be used and the brightness of the view field, the exposure unit suggests to the operator an appropriate exposure time to get a good photo of the sample. For our experiment a plan achromate objective D plan 10x giving, together with the eyepiece WHK 10x, a magnification factor of 100 was used. Diameter of view field was 2 mm, giving a scan area of just over 3 mm^2.

To measure the unknown optical densities the microscope–exposure unit system had to be calibrated first. For this purpose the step wedge, now having the known optical densities, was taken to the microscope and each step was regarded as normal sample. Keeping fixed the parameters like intensity of the light I_m, film format and ASA setting, reciprocity failure correction value etc., the suggested photographic microscope exposure times t_{mi} were read for each step of the step wedge. For microscope exposure E_{mi} we can write the relationship

$$\log E_{mi} = \log (I_m \times t_{mi}) = C_m + \log t_{mi} \quad [2]$$

where C_m is a constant different from C_E. When comparing relations [1] and [2] one becomes aware of their similarity and comes to the following logic: Logarithms of the exposures E_i are related to the optical densities D_i via the sigmoid H and D curve. In the opposite process, which happens in the microscope–exposure unit system, the exposure times t_{mi} are determined for the blackennings D_i of the step wedge which already intrinsically contain the sigmoid behaviour. So, a linear relationship between D measured by the densitomenter and t_m is expected.

Once the calibration procedure was performed, the unknown optical densities could be determined using the correlation graph for the exposure times suggested by the microscope exposure unit.

Several sets of gamma camera uniformity flood images in a wide range of count densities (45-4550 counts/cm^2) were recorded using a Microdot multiformat camera. All the images were recorded in the same format but varying the intensity setting on the CRT of the multiimager. All other parameters, like contrast and persistence of the screen, were kept fixed, granting in this way constant and reproducibile screen light conditions in the experiment. The films were developed in Agfa Gaevamatic 60 film processor under standard already mentioned conditions. The suggested exposure times were determined as an average of five readings across the area of every image and corresponding optical densities were read from the calibration graph. The film characteristic curves appropriate for use in nuclear medicine were produced.

Results – Two step wedges were exposed and analyzed to get the calibration curve as good as possible. The results in Fig. 2 show that there is a very good linear relationship between the data obtained by the microscope exposure unit (log t_m) and those measured by the transmission densitometer (D). The coefficient of correlation is as high as 0.999.

Table 1, as one example, contains the basic data in the process of scintigraphic sensitometry as described above. The scintigraphic characteristic curve derived from the data in Table 1 is

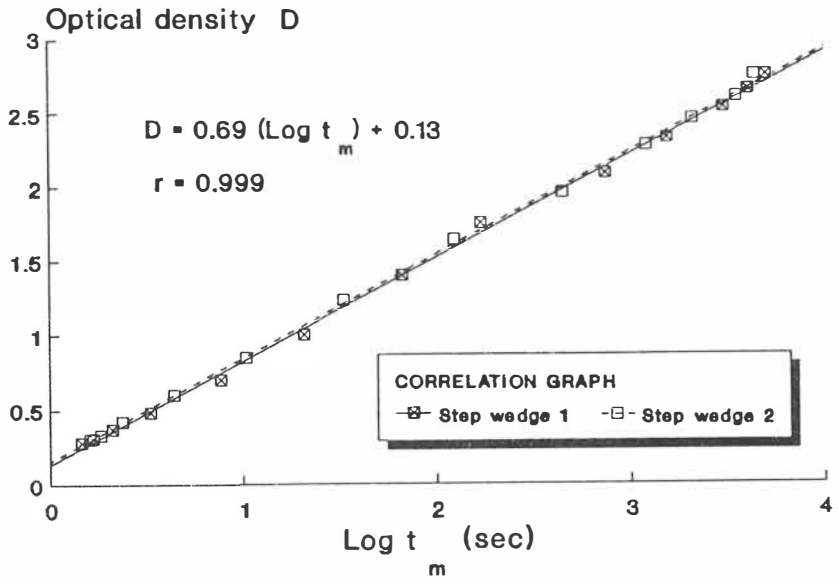

Fig. 2 -- Correlation of the transmission densitometer readings (optical densities, D_I) and microscope exposure unit readings (suggested exposure times t_{mi}) for two step wedges. The relationships are strictly linear.

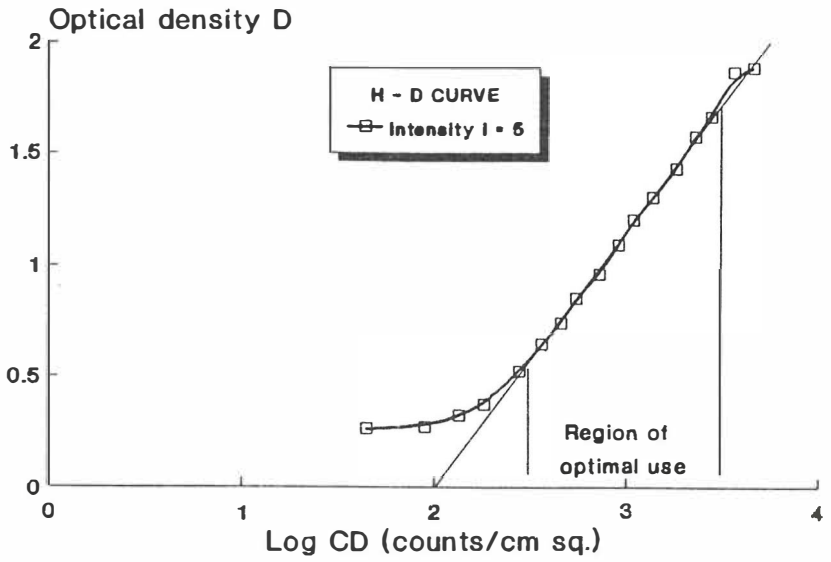

Fig. 3 – Scintigraphic characteristic curve obtained by analyzing a set of gamma camera uniformity flood images containing different count densities CD (Intensity setting I = 5).

shown in Fig. 3. It has, again, a typical sigmoid shape, but this time on X–axis we have logarithms of count densities, which is a parameter very common in nuclear medicine.

The linear part of the curve defines the region application and optimal use of the film in given conditions. In our example desribed by Table 1 and Fig. 3, the curve is linear for $2.49 < \log CD < 3.43$. By taking antilogarithms we find that for the film used, for intensity setting 5 on the Microdot imager and for given standard conditions of film development, the results will be good

and reliable if the count densities are in the range from 310 counts/cm^2 to 2 730 counts/cm^2.

In Fig.4 the dependence of the scintigraphic characteristic curves on the multiformat camera intensity setting is given. Evidently, it is a strong dependence, showing that for low intensity settings maximal optical densities (deep blacks) can not be achieved even for very high count densities. So, even the shape of the curve is somewhat different. The explanation is as follows: The sensitivity of silver halide grains to exposure light is usually regarded as a two–stage process. In the primary process which results in latent image formation one speaks in terms of «quantum yield» defined by the reciprocal of the number of absorbed quanta which are necessary to make a grain developable (1). At the very low intensity settings quantum yield is sometimes so small that in the secondary process of development lower optical densities are achieved despite the high amplication factor (The order of 10^9 silver atoms are produced for each stable silver atom in the latent image). Increasing the intensity setting the curves become steeper, narrowing in this way the region of optimal use of the film, while at the same time, maximal optical densities are only a little bit higher.

Table 1 – Basic data in the process of scintigraphic sensitometry. The t_m values in the third column are the means of five reading across each image area.

FLOOD IMAGE No.	COUNT DENSITY (counts/cm^2)	t_m(sec)	D
1	45	1.53	0.26
2	90	1.60	0.27
3	136	1.89	0.32
4	182	2.17	0.37
5	273	3.60	0.52
6	364	5.87	0.64
7	455	7.60	0.74
8	546	9.40	0.85
9	729	15.87	0.96
10	911	24	1.09
11	1092	36	1.20
12	1366	53	1.30
13	1821	66	1.43
14	2277	122	1.57
15	2732	168	1.69
16	3643	315	1.86
17	4553	348	1.88

Discussion – The plot of optical film density vs. logarithm of the count density, designated as scintigraphic characteristic curve of the film in nuclear medicine, is easily obtained by means of a calibrated microscope exposure unit. It is very applicable and useful in nuclear medicine beacuse it helps to determine the best working conditions in a very simple way.

The slope of the curve will depend on many parameters and so will, consequently, the optimal region of use of the film. The effect of the

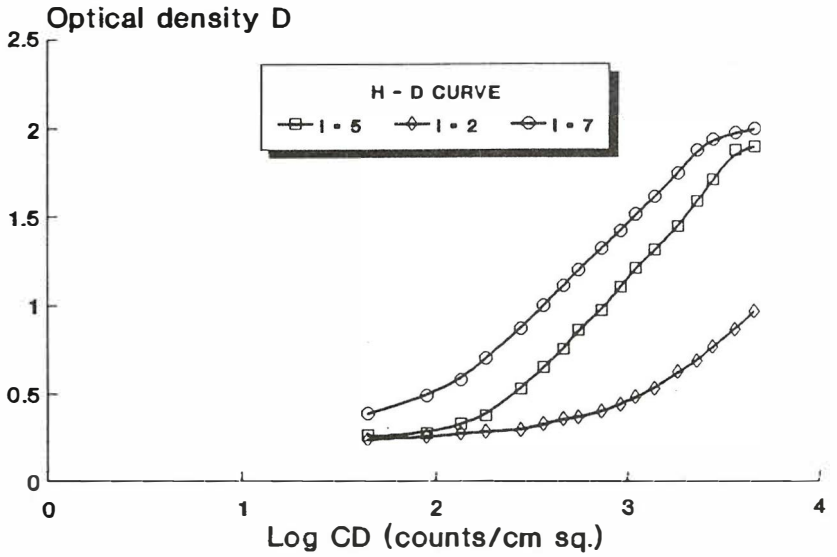

Fig. 4 – Dependence of the scintigraphic characteristic curves on the intensity setting of the multiformat camera.

following parameters is currently being studied: type of the film and multiformat camera, format of the images, effect of the high count rates because of the reciprocity failure (8), conditions of development etc.

It should, however, be very important and useful to fix the parameters and standards for film testing in nuclear medicine applications on an international basis which would enable the interlaboratory comparison (when working on same type machines) giving better quality in diagnostic nuclear medicine.

Sažetak

SCINTIGRAFSKA SENZITOMETRIJA FILMA I KONTROLA KVALITETE SLIKE U NUKLEARNOJ MEDICINI POMOĆU MIKROSKOPA

Osjetljivost filma i njegova karakteristična krivulja obično se određuje eksponiranjem, tzv. sivog klina pomoću svjetlosti standardne temperature boje i razvijanjem filma pod strogo definiranim i pažljivo kontroliranim uvjetima. Radiografski se filmovi testiraju, također, eksperimentiranjem plastičnog klina pomoću penetrirajućih X–zraka u standardnim uvjetima. Za denzitometrijska očitanja koriste se skupi denzitometri. Tako dobivene karakteristične krivulje filma ne sadrže, na žalost, dovoljno podataka od interesa za nuklearnu medicinu gdje se obično sa katodnog osciloskopa fotografiraju distribucije svjetlosnih impulsa različite prostorne gustoće i vremenske učestalosti. Da bi denzitometrijski rezultati imali smisla, način eksponiranja filma mora odgovarati načinu konačne upotrebe filma.

U ovom se radu umjesto denzitometra za indirektno određivanje optičke gustoće eksponiranog i razvijenog filma koristi jedinica za kontrolu ekspozicije citološkog mikroskopa. Dobivena je odlična korelacija između vrijednosti optičkih gustoća očitanih na visokokvalitetnom denzitometru i sugeriranih vremena ekspozicije za snimanje pomoću mikroskopa.

Niz slika ravnog uniformnog izvora radioaktivnosti snimljen je u uvjetima različite gustoće impulsa, što daje različita zacrnjenja. Scintigrafskom senzitometrijom uz pomoć mikroskopa dobivene su visokokvalitetne karakteristične krivulje filma, gdje je optička gustoća prikazana o ovisnosti o logaritmu broja impulsa po cm^2 predmeta. Analizirani su različiti parametri koji mogu utjecati na oblik krivulje i istaknuta potreba za uvođenjem izvjesne standardizacije ovakvih testova radi mogućnosti interlaboratorijske komparacije.

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EFFECT OF CONSTANT BACKGROUND ON GAMMA CAMERA UNIFORMITY AT DIFFERENT COUNT RATES

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Abstract – Flood field uniformity control has been widley accepted as the principal quality control test of gamma cameras. The uniformity indices are supposed to be the best (the lowest in value, according to NEMA) at low observed count rates where there is little difference to the true count rates.
In this work intrinsic uniformity was measured in a wide range of count rates for two most frequently used radionuclides, technetium–99m and iodine–131 to include the effect different energies. Although the uniformity is worse at high count rates, in a very busy nuclear medicine department, precautions may also be needed when the test is peformed at extremely low count rates. In the case of a very weak radioactive source of Tc–99m the indices of both integral and differential uniformity were found to be much higher than expected. At the same time, this unusual effect was not noticed when I–131 was used as a test source.
By eliminating other reasons, we suppose that the uniformity could possibly be affected by scattered radiation from I–131 used for numerous diagnostic tests in the same room. It is, normally, more evident in the studies of long duration.

UDC: 539-166.3

Key words: gamma cameras, quality control, uniformity, high count rate

Orig sci paper

Radiol Iugosl 1991; 25:251-4.

Introduction – Fast gamma camera electronics and the computer systems of great capabilities enabled extensive studies of the rapid biological processes in human subjects. At high count rates the pile–up of pulses may deteriorate the quality of an image due to wrongly positioned events. This is why the performance of the gamma camera at high count rate was studied by many authors, analyzing both the dead time of the camera (1) as well as image artifacts caused by high source activity (1, 2).

The flood field uniformity as one of the main parameters connected to the image quality was studied at a high count rate by Hasman and Groothedde (4). They have not found any dependence of the uniformity on count rate, which is in disagreement with our results as will be seen later. The indices of gamma camera non–uniformity as defined by Muehllehner et al. (5) and NEMA (6) were largely investigated (to a great extent) by Hughes and Sharp (7, 8). They studied (7) the effect of count density, photon energy and the use of energy correction circuitry on camera uniformity. In their second paper (8) they analysed the sensitivity of the uniformity indices (the ability to detect changes) as depending on count density, pixel size, smoothing etc. But they did not analyse the indices in the conditions of different count rates.

Our department is a very busy one. We have three gamma cameras in the same room. The camera under test in this work is surrounded by two others performing, among other diagnostic tests, cca 20 dynamic kidney scans with sodium I–131 orthoiodohippurate and several sodium 131–iodide bone scans per day. Another possible source of iodine background is the handy hot store used as the depository for vials containing radiopharmaceuticals to be applied.

Uniformity checks are done on all cameras at least once every day, but because of that relatively high I–131 background, ranging on that camera between 100-150 counts/sec, depending on detector head orientation (measured intrinsically with 20% window), we decided to measure the uniformity indices for different count rates and two different energies.

Materials and methods – For the experiment a Siemens ZLC–75, large field of view gamma camera (produced in 1981) was used. The detector head without collimator provided with a 3 mm thick lead ring mask was facing downwards because in that position the background count was minimum both for I–131 and Tc–99m.

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The point sources containing different activities of Tc–99m (or I–131) were put in the centre beneath the detector at the distance of 130 cm. The activities used were: for Tc–99m 4–330 MBq (100-8900 μCi), and for I–131 6–373 MBq (160-10090 μCi).

The data acquisition and analysis were done on an ADAC DPS 3300 computer. All the studies were acquired on the 64x64x16 matrix as recommended by NEMA and each time 30 million counts/image was collected (10000 counts/pixel). By doing so the stochastic component of the flood image non–uniformity, due to the random nature of radiation and to Poisson noise, was brought down to 1%. So, the flood image imperfections should reflect only the actual state of detector quality (9), except in the region of high count rates where the results may be influenced by the computer interface if the slow one is used. In this experimet the gamma camera and the computer were taken for one system. The computer interface working with the 9 MHz clock did not influence the results.

The built–in energy–linearity correction circuits of the gamma camera were actived all the time during the acquisition in the same way as during a normal patient study. The effect of high–count–rate (HCR) option was not investigated in this work. The energy window of 20% was used with centerline on 140 keV or 364 keV, depending on the choice of radionuclide.

The acqusition time varied from just over 5 min to approximately 50 min in the case of Tc–99m, and from 16 min to nearly 3 hours when I–131 was used as the test source. In both cases the physical decay was taken into account in such a way that the count rates were corrected to the middle of the time period.

The uniformity indices were calculated (according to the definition by NEMA, 1986) separately for UFOV (useful field of view) and CFOV (central field of view) as

$$\text{Integral.uniformity(\%)} = 100x \frac{(\text{Max-Min})}{(\text{Max+Min})}$$

where Min and Max represented the minimum and maximum pixel counts in the matrix and

$$\text{Differential.uniformity} = \pm 100x \left(\frac{\text{Largest.slice.deviation (Hi–Low)}}{\text{Hi+Low}}\right)$$

where Hi and Low were the highest and the lowest pixel counts over a range of 5 pixel in all rows columns.

Results – The behaviour of the camera-computer system at a high count rate for both radionuclides followed strictly the paralysable model as described by Muehllehner et al. (5), giving the maximum observed count rates of 95 kcounts/sec and dead time of 3.9μ sec for Tc-99m and 33 kcounts/sec and 11.2μ sec for I-131.

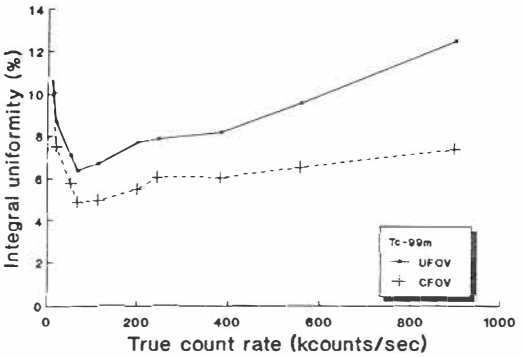

Fig. 1 – The indices of integral uniformity for useful and central field of view of the gamma camera as calculated for flood images taken with Tc–99m point sources giving different count rates.

The dependence of the integral uniformity for Tc-99m sources on the true count rate (not the observed one) is represented in Figure 1. The true count rate is the counting rate that would be recorded if the dead time of the system was zero. Integral uniformity is getting worse both in CFOV and UFOV with high activities applied, as it can be expected from our knowledge of pile-up effect. But, at the same time, the unexpectedly high values are noticed at very low count rates. When working with the activities of arround 100 μCi, the integral uniformity indices are nearly double than those one should expect when extrapolating the curves towards the low values of the true count rates.

A similar behaviour, although not so markedly expressed, of the differential uniformity for rows and columns of the matrix for Tc-99m sources could be seen in Figure 2.

The results of the same experiment, but using I-131 point sources, are given in Figures 3 and 4. One does not notice the adverse behaviour of the indices at low count rates. The true count rate range is different in these graphs because in the case of I-131 the saturation starts

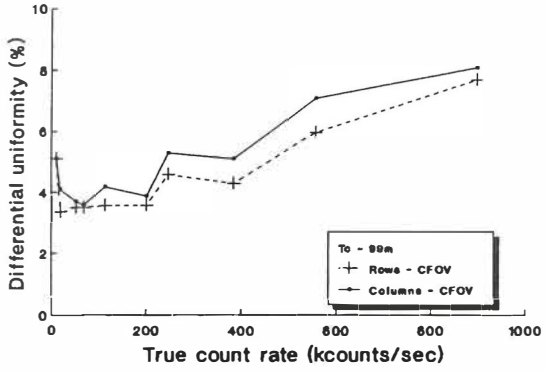

Fig. 2 – Differential uniformity in the CFOV vs. true count rate for Tc–99m point sources of different activites.

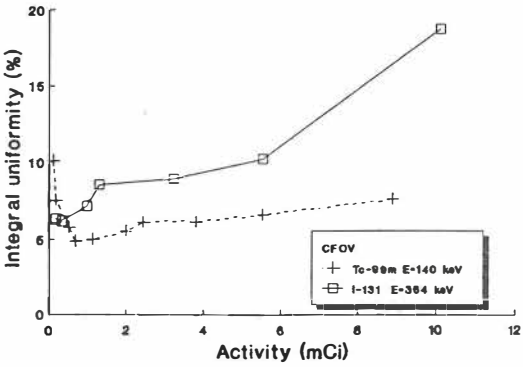

Fig. 5 – Integral uniformity in the CFOV sources of Tc–99m and I–131 as the function of increasing activity. A strong energy dependence is evident, especially at very high radioactivities.

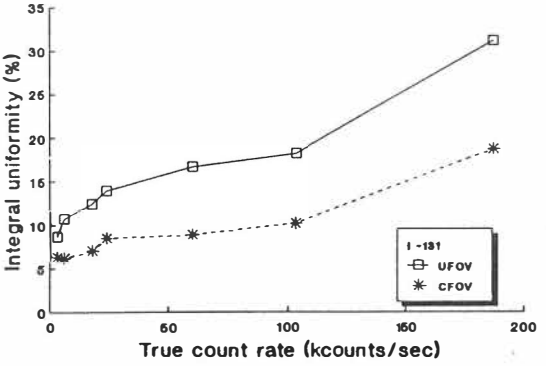

Fig. 3 – Integral uniformity for different true count rates in CFOV and UFOV using I–131 point sources.

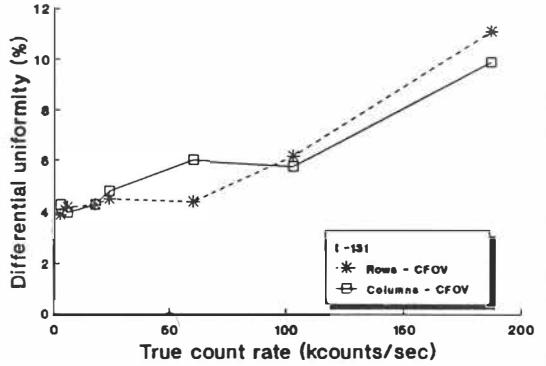

Fig. 4 – Differential uniformity in the CFOV vs. true count rate for I–131 point sources of different activities.

sooner due to the lower intrinsic efficiency of the crystal for higher energy gamma rays.

For the purpose of illustration and comparison in Figure 5, the true count rate values were recalculated back to activities. Evidently, there is strong dependence of the uniformity indices on the energy when high activities (and, consequently, high count rates) are applied: the uniformity is much worse in the case of I-131 than in the case of Tc-99m when the same activities are used for point sources.

Discussion and conclusion – The uniformity indices for constant count density flood images are increasing with increasing the true count rate (or activity of the source). This effect is stronger in the region of very high count rates where saturation and mispositioning of the events happen.

For equally radioactive sources, but of different gamma energy, worsening of uniformity with increasing the count rate (especially on its high side) will be much quicker in the case of the radionuclide emitting higher gamma energy.

The extraordinary high values of the indices were calculated for the flood images taken with very weak technetium sources. The unusual effect was not noticed when I-131 was used as a test source. The unusual effect is evidently time dependent, beeing most markedly expressed in the studies with the longest collection times. Analysing the conditions of the experiment, all the phenomena that would not cause a time dependent effect were eliminated as possi-

ble reasons for such a behaviour of the uniformity indices. The contamination of the detector with I-131 was also excluded.

We suppose that the uniformity could possibly be affected by scattered radiation from I-131 used in the same room for kidney or bone scans on other two cameras of beeing stored in the small hot depository. The low level of scattered radiation, with decreased photon energy and coming all the time from the same direction, could affect the uniformity only in the studies of long duration. Because of its decreased energy it falls out of I-131 energy window and produces no changes on I-131 flood images.

So, although in general the uniformity is better when measured at a low count rate, in a very busy nuclear medicine department precautions may also be needed when intrinsic uniformity tests are performed at low count rates (even not extremely low). That is why we suggest that in every busy department the uniformity indices be measured in the whole range of count rates (activities) in the standard set-up always used for intrinsic flood checks and then decide on the activity which is the most appropriate for everyday tests.

This work is still in progress. Changing the levels of constant I-131 background by using the sources of known activities in fixed positions as well as the effect of smoothing and off-peak flood imaging is being investigated.

Sažetak

UTJECAJ STALNOG POZADINSKOG ZRAČENJA NA UNIFORMNOST GAMA KAMERE KOD RAZLIČITIH BRZINA BROJANJA

Kontrola uniformnosti vidnog polja općenito je prihvaćena kao najvažniji test u programu kontrole kvalitete rada gama kamera. Indeksi uniformnosti uglavnom su najbolji (najniže vrijednosti, mjereno prema NEMA protokolima) kod malih brzina brojenja gdje je, normalno, mala razlika između registrirane i stvarne brzine brojenja.

U ovom radu indeksi uniformnosti mjereni su intrinsično u širokom rasponu brzina brojenja za dva najčešće korištena radionuklida tehnecij-99m i jod-131 da bi se uključio efekt različitih energija. Iako je uniformnost lošija kod velikih brzina brojanja, u jako zaposlenom zavodu za nuklearnu medicinu mjere predostrožnosti mogu biti potrebne i onda kad se test izvodi kod malih brzina brojenja. U slučaju vrlo slabog radioaktivnog izvora Tc-99m izmjereni indeksi integralne i diferencijalne uniformnosti mnogo su viši od očekivane vrijednosti. U isto vrijeme takav neobičan efekt nije zamijećen kad je I-131 korišten kao test izvor.

Eliminirajući druge potencijalne razloge za ovakvu pojavu, pretpostavljamo da se radi o kvarenju uniformnosti pod utjecajem raspršenog zračenja od I-131 koji se u istoj prostoriji koristi za brojne dijagnostičke testove ili stoji u priručnim »vrućim« spremištima. Utjecaj je, normalno, najevidentniji kod dugotrajnih studija.

Preporučamo da se u svakom jako zaposlenom nuklearno medicinskom zavodu indeksi intrinsične uniformnosti izmjere za široki raspon aktivnosti izvora i onda odluči koja je aktivnost najprimjerenija za rutinski svakodnevni test.

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SPLOŠNA BOLNIŠNICA MARIBOR, GASTROENTEROLOŠKI ODDELEK
ONKOLOŠKI INŠTITUT V LJUBLJANI

LASERSKO ZDRAVLJENJE STENOZANTNEGA RAKA POŽIRALNIKA

LASER TREATMENT OF STENOTIC ESOPHAGEAL CANCER

Pinter Ž, Pocajt M, Benulič T, Jančar B

Abstract – Laser treatment of stenotic cancer process in the esophagus has the potential of improving the quality of patient's life, and also enables further irradiation and/or chemotherapy. The method has proved effective in the prevention of cachexia and elimination of esophageal pain. When performed by an experienced endoscopist, the laser procedure is a realible method which entails only few complications. As such it is suitable also for patients in whom other treatment approaches are not feasible.

UDC: 616.329-006.6-089-073

Key words: esophageal neoplasms-surgery; laser surgery

Letter to editor

Radiol Iugosl 1991; 25:255-8

Uvod – Paliativni posegi pri malignih stenozah požiralnika imajo namen izboljšati kvaliteto življenja bolnikov, ki niso sposobni za radikalni operativni poseg. Z laserskim žarkom odstranimo mehansko oviro, ki bolniku preprečuje požiranje, in s tem zmanjšamo tudi bolečino. Z uspešno rekanalizacijo požiralnika preprečimo grozečo kaheksijo in omogočimo nadaljnje zdravljenje z radioterapijo in/ali kemoterapijo (1, 2, 3).

Cilj laserskega zdravljenja je odstranitev tumorske mase v lumnu požiralnika. Za poseg z laserjem smo se odločili pri bolnikih kjer operativni poseg ni bil možen zaradi lokalne razširjenosti tumorja, zasevkov po telesu in zaradi drugih spremljajočih bolezni. Zdravljenje z laserjem ni možno pri visoko ležeči stenozi, to je nad 15-18 cm od zobnega roba in pri ezofagealni fistuli.

Bolniki in metode dela – Od aprila 1987 do decembra 1990 je bilo na naš oddelek napotenih 40 bolnikov z napredujočim rakom požiralnika. Operativni poseg ni bil možen zaradi stenoze daljše kot 7 cm (pri 39 bolnikih), 13 bolnikov je imelo zasevke po drugih organih, 31 jih je bilo starejših od 60 let, od teh 20 starejših od 70 let. Pri 5 bolnikih je bilo prisotno še drugo, vzporedno rakavo obolenje.

Starost bolnikov je bila od 37 do 82 let, med njimi je bilo 8 žensk in 32 moških (slika 1).

Pri vseh bolnikih je bila diagnoza potrjena s histološko preiskavo biopsijskega materiala.

Zaradi izbire načina posega in orientacije v požiralniku smo pred pričetkom zdravljenja opravili še RTG slikanje prehodnosti požiralnika in CT zajetega področja. Dolžine rakaste rašče so prikazane na sliki 2. Stenozo v požiralniku smo opredelili glede na lego: v 1. tretjini požiralnika (1 bolnik), v 2. tretjini požiralnika (12) in v 3. tretjini požiralnika (27 bolnikov) (slika 2).

Posege z laserjem smo ponavljali v razmaku 2-3 dni, tako da smo dosegli prehodnost požiralnika za običajen gastroskop. Pri posegih smo uporabljali gastroskop firme Olympus GIP Q 10 in Neodym YAG laser firme MBB. Zožitev lumna smo ocenjivali pred prvim posegom in po zaključku zdravljenja z naslednjimi ocenami:

0 – lumen ni viden,
1 – lumen je viden,
2 – lumen 3-4 mm (širina biopsijskih kleščic),
3 – lumen 7-8 mm (širina biopsijskih kleščic),
4 –lumen 12-14 mm, prehoden za gastroskop.

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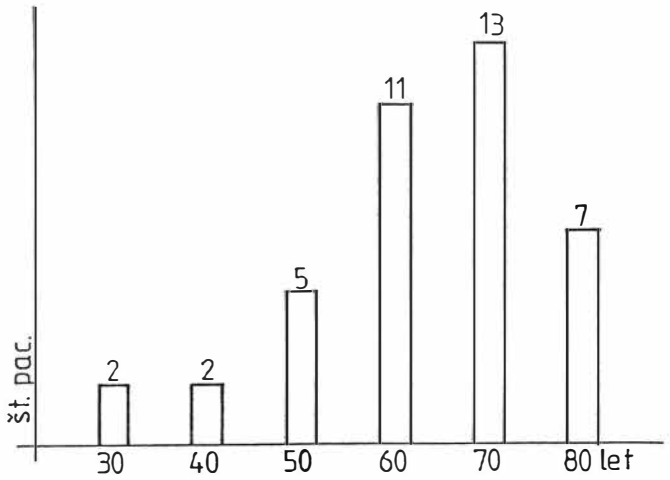
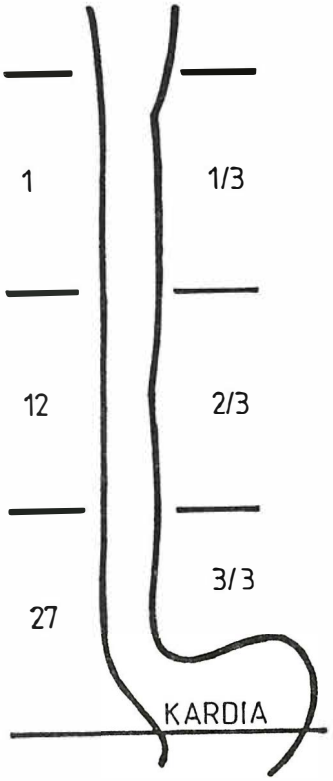
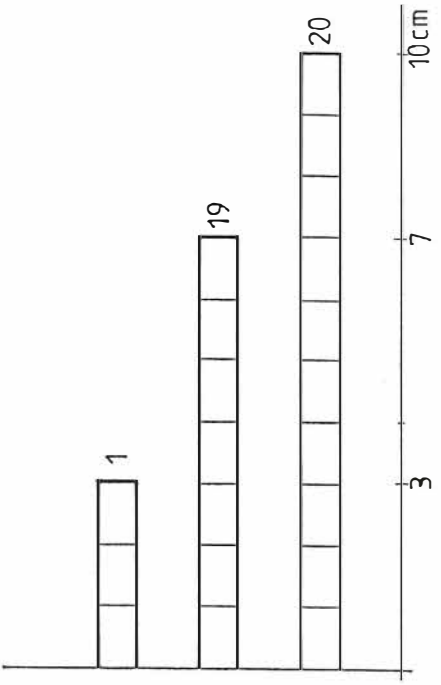


Slika 1 – Razdelitev bolnikov po starosti
Fig. 1 – Distribution of patients by age



Slika 2 – Lokalizacija raka v požiralniku po tretjinah
Fig. 2 – Localization of cancer in the esophagus by thirds



Slika 3 – Dolžina rakov v požiralniku
Fig. 3 – Extent (length) of esophageal cancer

Ocenjevali smo tudi sposobnost požiranja pred prvim posegom in po zaključku zdravljenja:

0 – ne more požirati,
1 – pije tekočino,
2 – pije brez težav,
3 – požira pasirano hrano,
4 – požira formirano hrano.

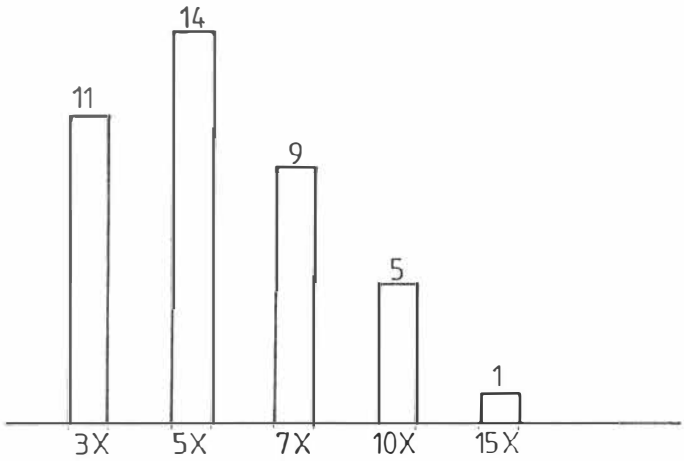
Rezultati – Pri 40 bolnikih smo opravili skupno 231 posegov z laserjem, povprečno 5,7 pri posameznem bolniku (1-15) (slika 4).

Prehodnost požiralnika in sposobnost požiranja pred in po zdravljenju so prikazani na sliki 5 in 6.

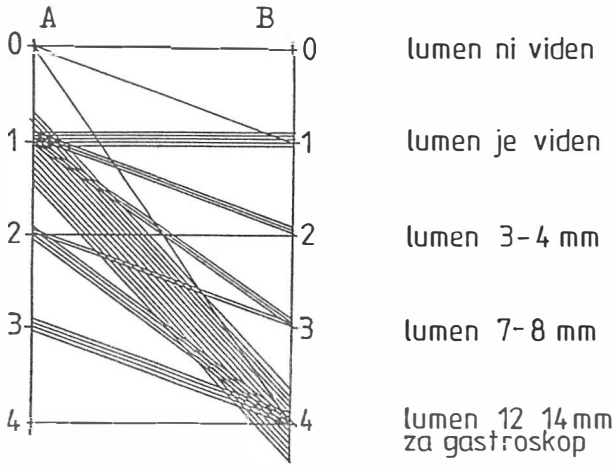
Preživetje bolnikov od posega z laserjem do smrti je prikazano na sliki 7.

Bolniki so bili hospitalizirani na oddelku povprečno 14 dni (4-28 dni).

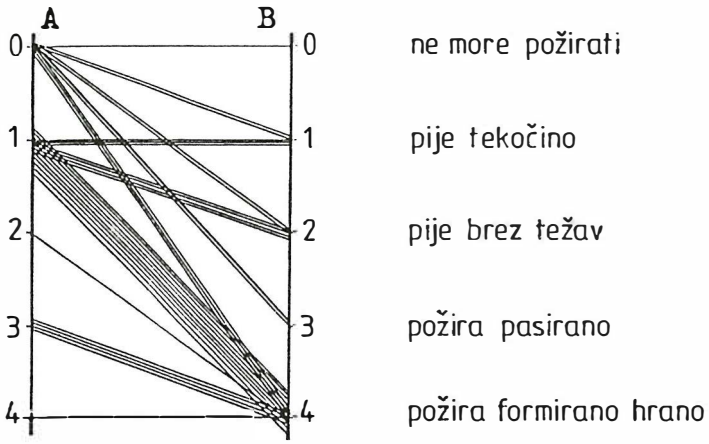
Komplikacije : Komplikacije, ki jih pri posegih z laserjem pričakujemo, so: perforacija in krvavitev pri bolniku in refleksija laserskega žarka ter fotokoagulacijski efekt na roženici očesa pri



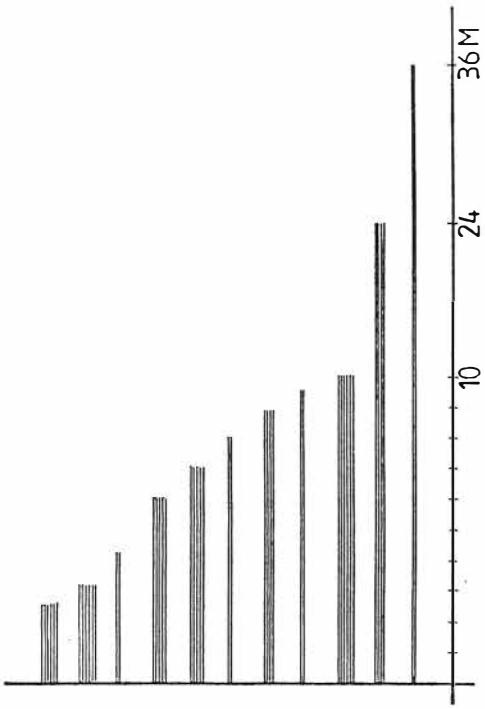
Slika 4 – Število posegov z laserjem pri bolniku
Fig. 4 – Number of laser interventions per patient



Slika 5 – Prehodnost požiralnika: A – pred zdravljenjem, B – po zdravljenju
Fig. 5 – Passability of esophagus: A – before treatment, B – after treatment



Slika 6 – Sposobnost požiranja: A – pred zdravljenjem, B – po zdravljenju
Fig. 6 – Swallowing ability: A – before treatment, B – after treatment



Slika 7 – Preživetje bolnikov po laserskem zdravljenju (v mesecih)
Fig. 7 – Survival of patients after laser therapy (in months)

endoskopistu in asistentih. Vseh komplikacij je bilo sedem (3% od 231 posegov) in to: tri perforacije, dve fistuli ter po enkrat zastoj dihanja in zapora lumna.

Ezofagealni fistuli sta nastali več tednov po zadnjem posegu z laserjem, tako da ju težko ovrednotimo kot neposredno komplikacijo zdravljenja. Do zastoja dihanja (pojavil se je enkrat in minil po ustrezni terapiji) lahko pride ob prekomerni analgetični terapiji, posebno pri starejših bolnikih, vendar, odkar uporabljamo preparat flumazelin, podobnih komplikacij ni bilo.

Zaključek – Ugotavljamo, da s paliativnim laserskim zdravljenjem izboljšamo kvaliteto življenja bolnikov z napredujočim rakom požiralnika. Ob primerni medikamentozni predpripravi bolniki dobro prenašajo zdravljenje. Laserski žarek je v rokah izkušenega zdravnika – endoskopista – varen inštrument in omogoča zanesljivo opravljan endoskopskih posegov tudi pri ogroženih bolnikih.

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ONKOLOŠKI INŠTITUT LJUBLJANA

EPIDEMIOLOŠKI POGLED NA PROBLEMATIKO RAKA V SLOVENIJI IN JUGOSLAVIJI

EPIDEMIOLOGICAL ASPECT OF CANCER RELATED PROBLEMS IN SLOVENIA AND YUGOSLAVIA

Pompe Kirn V

Abstract – Cancer morbidity in different republics of Yugoslavia varies according to the differences in age structure, life habits and socio-economic conditions. Relevant data on cancer incidence are available only for Slovenia, Croatia and Voivodina. In the remaining parts of Yugoslavia the registration is still being introduced and therefore their cancer incidence could be estimated on the basis of mortality data only. The obtained figures are, however, not representative due to the excessive load of prognostically unfavourable cancers; the data are influenced also by the quality of death cause determination which is varying by different republics.

In all republics a majority of cancer related deaths are due to lung cancer, which is followed by stomach- and breast cancers. The mortality rates for lung cancer in men and breast cancer in women are constantly increasing in all regions, and so are also the respective rates for cancers of the oral cavity, tongue, pharynx and larynx, as well as for colorectal cancer. The highest increase is observed in the incidence of cancers 70-80% of which are related to cigarette smoking.

In Slovenia and Yugoslavia as well, the endeavours to achieve 15% decrease of cancer mortality should be centred on well prepared campaigns against active and passive smoking, and against alcohol abuse; apart from these, sensibly organized and to our conditions adjusted secondary prevention, i.e. screening programs for the detection of precancerous and early stages of cervical and breast cancer are also expected to contribute to this goal. In 1991, two cancer prevention programs are under way in Slovenia: 1) Slovenia 2000 and Cancer, organized by the Slovenian Anticancer Society and the Institute of Oncology in Ljubljana, and 2) CINDI program carried out by the Health Center of Ljubljana.

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Letter to editor

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Uvod – Onkološka epidemiologija obravnava pojavnost raka in raziskuje vzroke njenih sprememb in različnosti po svetu. S pomočjo matematičnih modelov napoveduje spremembe. V njeno področje dela sodijo tudi intervencijske populacijske in klinične študije.

Epidemiologi opazujejo bolezen kot množičen pojav, za katerega veljajo zakonitosti statistike, ki temeljijo na teoriji verjetnosti. Zaradi vključitve statistike v epidemiološka proučevanja se metodologija dela hitro razvija. Problem opazovanja redkih pojavov na majhnem populacijskem območju, npr. opazovanja posameznih primerov levkemij v okolici različnih virov sevanja kljub vsemu prizadevanju še ni rešen.

V zadnjih letih je vse bolj prisotna težnja zlitja dognanj laboratorijske eksperimentalne onkologije, predvsem molekularne biologije z epidemiologijo. Večji mednarodni raziskovalni centri raka, kot je IARC (Mednarodna agencija za raziskavo raka) sodijo med njene pobudnike z organizacijo tečajev in skupnih raziskav.

Zbolevanje za rakom v posameznih republikah Jugoslavije

Zbolevanje za rakom v posameznih republikah Jugoslavije je glede na raznoliko starostno strukturo, življenske navade in različen socialno ekonomski razvoj, zelo različno. V predelih z večjim odstotkom starejših je raka več. Zato je pred iskanjem drugih vzrokov za razlike v obolevanju potrebno podatke najprej starostno standardizirati (1). Najboljša mera številčne ocene zbolevanja za rakom je incidenca. Zanesljive podatke o incidenci pa lahko dobimo le za republiki Slovenijo in Hrvaško ter Vojvodino, kjer imajo registri raka že dolgoletno tradicijo zbiranja in obdelave podatkov. Podatke o incidenci raka v Sloveniji in na Hrvaškem lahko redno poiščemo v letnih poročilih obeh registrov. V preostalih delih Srbije in v drugih republikah je registracija raka od 1. 1. 1986. dalje z zakonom predpisana in obvezna, vendar kot lahko razberemo iz poročila Zveznega zavoda za zdravstveno varstvo

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novembra 1990 (Izveštaj o prijavi malignih neoplazmi u SFRJ u 1988 godini) (2), je v teh predelih registracija raka nepopolna in so vrednosti incidence podcenjene.

Zvezni zavod za zdravstveno varstvo je v letu 1990 izdal še drugo gradivo: Smrtnost od malignih neoplazmi u Jugoslaviji 1969-1987 (3). Čeprav mortaliteta ni reprezentativen podatek o obolevnosti, zaradi prevelike teže prognostično neugodnih rakov in zaradi vpliva kvalitete zdravstvene službe na opredeljevanje vzrokov smrti, je to edini kazalec, ki ga po priporočilih SZO zbirajo skoraj v vseh deželah sveta. Za leto 1987. navaja Zvezni zavod za zdravstveno varstvo za Jugoslavijo kot celoto koeficient 145,3/100000 prebivalcev. S takšnimi vrednostmi dejanske in tudi starostno standardizirane umrljivosti zaradi raka se Jugoslavija uvršča skoraj na dno evropske lestvice. Od te povprečne vrednosti značilno odstopajo Slovenija, Hrvaška in Vojvodina z višjimi vrednostmi (207,3-202,2/100000), in se uvrščajo v sredino evropske lestvice. Značilno nižje vrednosti so na Kosovu, v Črni Gori in Makedoniji (35,8-88,3/100000).

V vseh republikah je bilo največ smrti zaradi pljučnega raka. Najvišji koeficienti so bili v Vojvodini, na Hrvaškem in v Sloveniji. Primerjava podatkov iz let 1969, 1973, 1979, 1983 in 1987 kaže, da povsod narašča umrljivost za pljučnim rakom. Razmerje med spoloma (moški/ženski) je bilo v Jugoslaviji povprečno 6 : 1, največje na Hrvaškem in v Vojvodini (9:1). Želodčni rak je bil kot vzrok smrti med raki na drugem mestu, čeprav se koeficienti povsod, razen v Bosni in Hercegovini ter Črni Gori, manjšajo. Razmerje med spoloma je bilo 3 : 2 za moške. Ženske v vseh predelih Jugoslavije umirajo vseveč zaradi raka dojk. Najvišja umrljivost je bila leta 1987 v Sloveniji, Vojvodini in na Hrvaškem (33,9 – 21,8).

Povsod je naraščala umrljivost zaradi raka grla, žrela, jezika in ustne votline, rektuma in debelega črevesa. Zaskrbljujoče je, da je v Jugoslaviji leta 1987 še vedno 737 žensk umrlo zaradi raka materničnega vratu. Povprečni koeficient je znašal 6,2/100000, najvišji je bil v Srbiji (10,9/100000 na ožjem območju in 8,4/100000 v Vojvodini). Glede na leto 1979 in 1983 so koeficienti na Hrvaškem porasli, v Sloveniji so se stabilizirali, v Srbiji so upadli. Koeficienti so nekoliko porasli v Črni Gori, v Makedoniji in na Kosovu, vendar so bile zabeležene vrednost (1-2/100000) povsod precej nižje od jugoslovanskega povprečja.

Nižje vrednosti mortalitete, četudi so starostno standardizirane, ne pomenijo dejansko nižje umrljivosti v primerih, ko je odstotek slabo opredeljenih vzrokov smrti velik, npr. 30% na Kosovu in 25% v Črni Gori. V teh primerih je mortaliteta zaradi raka gotovo podcenjena.

Možnosti primarne in sekundarne preventive

Namen prispevka ni v povdarjanju razlik v obolevnosti in umrljivosti, ampak v iskanju skupnih opornih točk za boljšo organizacijo primarne preventive in zgodnjega odkrivanja tistih rakavih bolezni, kjer rizične dejavnike poznamo premalo, da bi jih lahko aktivno preprečevali.

Upoštevajoč dolgo latenčno dobo večine rakavih bolezni, znanje o rizičnih dejavnikih in o redu velikosti njihovega vpliva, razvite dežele Severne Amerike, dežele Evropske gospodarske skupnosti in nordijske države s pomočjo večjih raziskovalnih centrov načrtujejo, uvajajo in merijo uspešnost primarnih preventivnih programov.

Članice Evropske gospodarske skupnosti so sestavile skupino strokovnjakov za pripravo predloga programa »Evropa proti raku« januarja 1986 (4). Leto 1989 so proglasile za informativno leto o raku in izdale Evropski kodeks proti raku, ki obsega deset znamenitih zapovedi. Izpolnjevanje teh zapovedi naj bi do leta 2000 zmanjšalo umrljivost za rakom za 15%.

Največ si obetajo predvsem od uspešnega boja proti aktivnemu in pasivnemu kajenju. Epidemiološke raziskave so pokazale, da bi se s prenehanjem kajenja lahko izognili 80 – 90% pljučnega raka pri moških, 60-80% pljučnega raka pri ženskah, 30-70% raka mehurja, 30-40% raka ledvic in 30% raka trebušne slinavke. Ob prenehanju kajenja in zmanjšanju uživanja alkoholnih pijač bi lahko zmanjšali obolevnost in umrljivost za rakom grla in požiralnika za 75%, za rakom jezika, ustne votline in žrela pa za 85% (5).

V izogib malignemu melanomu in drugim kožnim rakom odsvetujejo pretirano sončenje. Priporočajo omejevanje števila rentgenskih pregledov in upoštevanje varnostnih predpisov pri proizvodnji, skladiščenju in uporabi karcinogenih snovi.

Za področje prehrane, kjer so dognanja epidemiologije in bazične onkologije še skromna, dajejo splošna navodila: priporočajo predvsem biološko polnovredno, uravnoteženo prehrano brez kaloričnih viškov, fizično aktivnost in vzdrževanje ustrezne telesne teže.

V vseh predelih Jugoslavije predstavljajo kadilski raki velik delež rakov pri moških. V Sloveniji narašča število teh rakov pri moških srednjih let, tako da v Registru raka registriramo največ pri-

merov pljučnega raka in rakov grla, žrela in ustne votline med 50 in 64 letom starosti. Največji porast incidence opažamo prav pri rakih ustne votline, jezika, žrela in grla (6). V Sloveniji boj proti kajenju še ni dovolj dobro organiziran. Obstaja nekaj društev nekadilcev, omejitev kajenja na sestankih in v nekaterih javnih prostorih, vendar je pravica nekadilcev do čistega zraka še vse premalo spoštovana. Alkoholizem je v Sloveniji velik družbeni problem.

Tudi organiziranega presejanja (screening) za zgodnje odkrivanje raka materničnega vratu v Sloveniji še ni. Incidenca invazijske oblike tega raka je že deset let 17/100000 žensk in umrljivost 6/100000 žensk. V Sloveniji so še vedno območja z incidenco okoli 30/100000 in umrljivostjo okoli 10/100000 (obalne občine). V starosti 60-69 let incidenca narašča, v starosti 60-64 let je povprečni letni porast celo 5,4%. Ženske hodijo na preventivne ginekološke preglede po lastni presoji, nekatere prepogostokrat, druge, bolj ogrožene pa premalo ali nikoli. Potrebno bo uvesti presejanje v pravem pomenu besede za ženske stare 27-55 let na vsaka tri leta po dveh zaporednih negativnih brisih (7). Skrbna merjenja uspešnosti presejanja drugod po svetu so pokazala, da lahko s takšnim pregledovanjem znižamo umrljivost zaradi raka materničnega vratu do 90%.

Ker je problematika raka dojk posebno v nekaterih predelih Slovenije zelo velika (incidenca je v ljubljanskih občinah okoli 100/100000 žensk), poteka v organizaciji Onkološkega inštituta v Ljubljani od leta 1989 randomizirana pilotska študija v šestih občinah. Ženske stare 50-64 let so vabljene na klinični pregled in mamografijo. Rezultati študije bodo vodilo pri morebitnem uvajanju sistematičnih pregledov v najbolj prizadetih občinah (8). Umrljivost zaradi raka dojk se lahko zniža od 35% do 40% (5), če je le odzivnost žensk na ponujene programe dovolj velika – 40% smrti manj pri najbolj pogostnem raku žensk v Sloveniji bi pomenilo veliko število rešenih življenj.

Kaj je bilo od navedenih možnosti storjenega v Sloveniji? Zveza slovenskih društev za boj proti raku je s pomočjo zdravnikov Onkološkega inštituta preoblikovala Evropski program v program Slovenija 2000 in rak. Izdala ga je sredi leta 1990 (9). Pri tem je deset evropskih zapovedi spremenila v Sedem dobrih nasvetov in jim dodala še Sedam znamenj, oboje v obliki ličnega letaka. V letu 1991 je izšlo posebno gradivo za učitelje osnovnih in srednjih šol. V programu so zapisali, da Zveza slovenskih društev za boj proti raku in Onkološki inštitut, pobudnika in nosilca programa organizirata izobraževanje in vzgojo celotnega prebivalstva Slovenije, konkretno v osnovni šoli, ki jo osem do dvanajst let obiskuje vsak Slovenec. Sodeluje tudi Rdeči križ ki ima zdravstveno vzgojo predvideno v svojem programu in s svojimi organizacijami sega skoraj v vsako našo vas. V tednu boja proti raku so Univerzitetni zavod za zdravstveno varstvo. Zavod RS za šolstvo, Republiški odbor Rdečega križa Slovenije, Zveza društev nekadilcev ter Onkološki inštitut podpisali dogovor o izvajanju tega programa. V aprilu so stekli prvi tečaji za zdravnike in višje medicinske sestre. Zdravniki bodo poučevali učitelje, ki bodo, tako kot višje medicinske sestre, posredovalci programa. Štirje člani kancerološke sekcije po predahu več kot 15 let spet obiskujejo regijska kancerološka društva in regijske podružnice SZD z izbranimi prispevki iz onkologije. Poslušavci (zdravniki) najčešče želijo odgovor na vprašanja iz njihovega vsakdanjega dela z onkološkimi bolniki in iz lokalne ekološke problematike.

Lahko rečemo, da je zagnanost predavateljev na tečajih in obiskov na terenu zaenkrat še dovolj velika. Sprašujemo pa se, če smo na pravi poti in delamo času primerno. Prav gotovo je vsak začetek težak in upamo, da bomo speljali evropski program tudi v našem prostoru navkljub težkim časom. Pri tem ne smemo pozabiti, da je evropski program široko zasnovan in da poleg zdravstvene vzgoje prebivalstva vsebuje še: preprečevanje raka, izobraževanje zdravstvenih delavcev ter raziskovalno delo. To so kompleksne naloge, ki zahtevajo timski pristop strokovnjakov različnih strok (4). Tudi za zdravstveno vzgojo prebivalcev in preusmerjanje njihovih življenskih navad bi bilo potrebno storiti več; po zgledu nekaterih uspešnih reklam v večji meri prodreti v najbolj razširjene medije obveščanja: radio, televizija, seveda ne amatersko, temveč v sodelovanju s psihologi, novinarji in vsemi tistimi, ki obvladajo tehniko sodobnega širjenja novic. Zelo poslušane kontaktne oddaje bi morali skrbneje pripraviti. Pametneje je javno povedati, da je danes onkologija zelo široko področje in da vsak zdravnik Onkološkega inštituta ne more obvladati celotne onkologije; potem se ne bi zgodilo, da bi izpadli kot nepoznavalci, ko bi hoteli povedati nekaj, kar ni več v skladu s sodobnimi dognanji.

V Ljubljani poteka program CINDI, ki ga po navodilih in metodologiji SZO izvaja Zdravstveni dom Ljubljana. To je širše zasnovan preventivni program, ki vključuje vse točke programa Slovenija 2000 in Rak. Ali smo se medsebojno dovolj povezali? Ali bomo pri vzporednih preventivnih

akcijah v Sloveniji pametno sodelovali? Kako bomo merili uspešnost? S programom CINDI je ocenjeno izhodiščno stanje na vzorcu prebivalcev Ljubljane, Onkološki inštitut ima že rezultate raziskave javnega mnenja iz leta 1989 (10).

Kaj bomo dosegli leta 2000? Bojim se, da glavnega kazalca zaželjenega cilja, to je zmanjšanje umrljivosti za rakom za 15% še ne, saj tega v tako kratkem času tudi realno ne moremo pričakovati. Veseli bomo lahko, če bo ponovljena raziskava javnega mnenja leta 2000 pokazala, da je v starosti 20-40 let manj kot 50% kadilcev med moškimi in manj kot 40% kadilk med ženskami. Toliko jih je po podatkih raziskave javnega mnenja bilo leta 1989. Veseli bomo tudi, če bomo v Registru raka za Slovenijo namerili večjo incidenco neinvazivnih intraduktalnih rakov dojk in več primerov intraepitelijske oblike raka maternicnega vratu med ženskami po 40.letu starosti. Potem bomo lahko upali, da bodo čez nekaj let tudi rezultati merjenja umrljivosti zaradi raka ugodnejši.

Povzetek – Zbolevanje za rakom je v posameznih republikah Jugoslavije glede na različno starostno strukturo, različne življenjske navade in različen socialno ekonomski položaj različno. Reprezentativni podatki o incidenci raka so na voljo le za Slovenijo, Hrvaško in Vojvodino. V ostalih območjih Jugoslavije se registracija šele uvaja, zato lahko ocenjujemo incidenco le iz podatkov o umrljivosti. Te ocene zaradi prevelike teže prognostično neugodnih rakov niso reprezentativne; nanje vpliva tudi kvaliteta opredeljevanja vzrokov smrti, ki je v posameznih republikah različna.

V vseh republikah je največ smrti zaradi pljučnega raka, na drugem mestu je želodčni rak, na tretjem rak dojk.

Umrljivost zaradi pljučnega raka pri moških in raka dojk pri ženskah narašča povsod, enako tudi umrljivost zaradi raka ustne votline, jezika, žrela in grla ter danke in debelega črevesa. Najbolj naraščajo raki, ki jih v 70-80% pripisujemo kajenju.

V boju za 15% zmanjšanje umrljivosti zaradi raka si tudi v Sloveniji in Jugoslaviji lahko največ obetamo od dobro pripravljenih akcij zoper aktivno in pasivno kajenje in zoper alkoholizem ter v premišljeni, našim pogojem prilagojeni organizaciji sekundarne preventive, tj. presejanja (screening) žensk za prekancerozne spremembe in zgodnje stadije raka maternicnega vratu in dojk. V Sloveniji potekata v letu 1991 dva preventivna programa: Slovenija 2000 in rak, v organizaciji Društva za boj proti raku in Onkološkega inštituta in Program CINDI v organizaciji Zdravstvenega doma Ljubljana.

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INTERREGIONAL TRAINING COURSE ON NUCLEAR MEDICINE

organized by IAEA

held at the Nuklearmedizinische Klinik Klinikum Berlin Buch, Germany
September 16 – October 11, 1991

The Training Course was organized and financed by the International Atomic Energy Agency (IAEA), Vienna in cooperation with the World Health Organization and Ministry of Research and Technology of the German government, Bonn.

The program of the Course included theoretical and practical training in general clinical application of radionuclides in medicine (diagnostic and therapeutic), safe handling of radioisotopes, data analysis for *in vivo* and *in vitro* investigations with radionuclides and organization of radiation protection and radiopharmacy services in nuclear medicine practice.

The Course also acquainted the students with some of the recent advances in nuclear medicine such as immunoscintigraphy and positron emission tomography.

Prof. H. Deckart, who was the Course director and chairman of all sessions, should be mainly credited for the excellent perforrnance of the course.

It would be impossible to mention all the speakers – internationally renowned professionals – whose lectures enriched the knowledge of participants on particular topics, and who were always ready for discussion, additional explanations and confronting of ideas. Nevertheless, I should mention at least some of them.

In the first part of the Course, which was dedicated prevailingly to basic research and *in vitro* investigations, we had the opportunity to attend lectures on radiopharmaceuticals by **Prof. G. Subramanian** from New York and **Dr. S. Hesslewood** from Birmingham. The lectures of **Dr. R. Piyasena were centred on radioimmunoassay, quality controls and, nevertheless, on the possibilities of progress in developing countries.**

The second part of the Course was more clinically oriented. There we had the opportunity to enjoy the excellent lecture on investigations in nephrology by Dr. K. Britton where clearly delineated principles were presented along with further perspectives of these functional investigations. He also reported on their experience with radioimmunotherapy (intraabdominal applications) and the use of MIBG in neuroblastoma therapy, with emphasis on the importance of MIBG as a first-line therapy. Namely, chemotherapy often causes dedifferentiation of tumors which renders MIBG treatment ineffective. The cases of patients with advanced disease who have been cured point out, however, that the problem of radiation protection is worth solving, and that the treatment should be started in due time.

In his lecture **Prof. J. F. Chatal** from Nantes gave a clear review of tumor markers, whereas **Prof. E. Pauwels** from Leiden lectured on the diagnostics of arthritis and on thyroid scintigraphy.

Diagnostic procedures in thyroidology and thyroid oncology with all dilemmas were excellently reviewed and summarised from other lectures by **Prof. H. Deckart** from Berlin. He emphasized the importance of team work in the diagnosis and treatment of thyroid diseases, which is essential for optimum results.

Apart from his investigations in hematology, **Dr. K. Buchali** from Berlin had theoretical and practical presentation of his experience with preoperative lymphscintigraphy in malignant melanoma; using this method, corresponding surgery in high risk patients (Clark III – V) resulted in a 20% improved disease free survival. The analysis of their results of double blind study with 89-strontium therapy or saline as placebo was also interesting. They have treated skeletal metastases of prostatic carcinoma and, unexpectedly, beside the effect on pain a higher survival rate was found after Sr application.

Prof. U. Buell from Aachen had an interesting presentation on Nuclear Imaging Techniques in Brain.

Many speakers had lectures related to cardiology, among them also **Prof. A. Cuaron** from Vienna (IAEA) who joined us during the last week of the Course. His clearly defined standpoints on furthering nuclear medicine in developing countries and final panel discussion were met with great interest.

The scope of the Course covered a large variety of topics, among them also the following: dosimetry, radiation protection, instrumentation in nuclear medicine, adverse reactions to radiopharmaceuticals, quality assurance at all levels of nuclear medicine, endocrine orbitopathy, diagnostics in inflammatory diseases, regular aspects of drug regulations, SPECT, PET, clinical use of stable isotopes, P-32-treatment of Polycythemia vera, nuclear medicine in hepatology, radiosynovorthesis in rheumatoid arthritis, diagnostic procedures in endocrinology, pediatric nuclear medicine, recommendations of IAEA, etc.

As it has been impossible to mention all the speakers, it is also far beyond the scope of this brief report to enlist all the questions, problems and topics that have been presented and/or discussed at the Course.

Every afternoon was dedicated to a laboratory course with practical training. Here we should specially point out the outstanding kindness and hospitality of the staff of Nuclear Medicine Clinic in Berlin-Buch. They were always open for discussion and willing to provide extra information when needed. They never objected when a participant would express his interest in additional training. Without their help this training would not have been possible.

All the participants received a lot of additional literature (drafts of lectures and articles). Last but not least, IAEA provided us with a draft of the Handbook of Nuclear Medicine Practice in Developing Countries (Figure 1).

We were enabled to visit the Nuclear Medicine Department in Berlin-Zehlendorf City Hospital with demonstration of pulmonary function; Nuclear Medicine Clinic of the Charité Hospital in Berlin, as well as the Nuclear Medicine Department of Friedrichshein-Hospital, Berlin, with lecture on Nuclear Medicine Emergency Diagnostics.

We also had an interesting scientific excursion organized to the Reactor Center in Rossendorf near Dresden.

The social program was very rich, despite the tough schedule. Thus we had the opportunity to see Potsdam with Prussian Kings' Gardens and Palaces (Sanssouci, Cecilienhof), Bernau, Dresden with the King's palaces, galleries and Königstein, as well as Sächsische Schweiz (Elbsandsteingebirge) and Rembrandt exhibition.

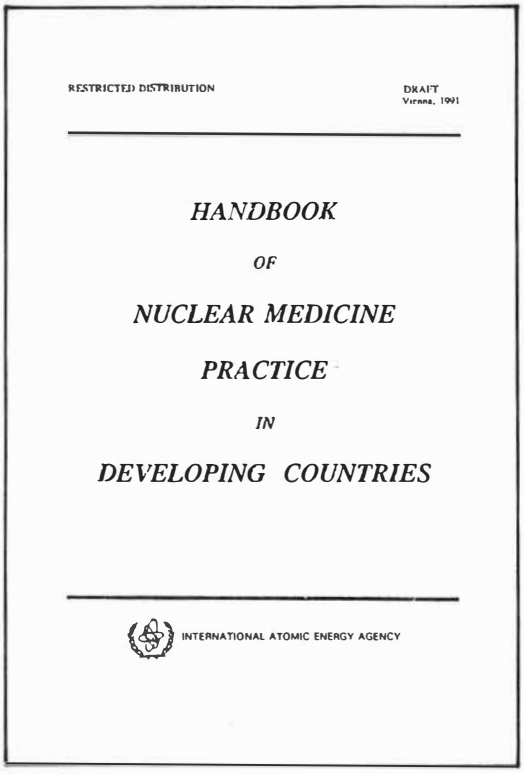
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Fig. 1 – Part of literature which was given to the participants at the course

The participants were from 24 different countries world-wide, Europe, Asia, Africa and Latin America. By the end of the Course it was our generally belief that, apart from gaining additional professional knowledge, we got useful ideas how to improve our routine diagnostic and treatment methods together with guidelines for our further research work.

The Course has confirmed that nuclear medicine remains an indispensable part of in vitro and in vivo diagnostics and therapy so in the developed as well as in developing countries.

Undoubtedly, in organizing this Course, IAEA has not just met but actually surpassed the expectations of participants. Finally, thanks to the Agency, almost all participants received fellowships which enabled them to attend this valuable professional training.

Viljem Kovač, MD

EUROPEAN SCHOOL OF ONCOLOGY
The Institute of Oncology and the Faculty of Medicine
Ljubljana, Slovenia, Yugoslavia

Preliminary Announcement

2nd Rare Tumor Symposium

MALIGNANT MELANOMA AND PREGNANCY

Thursday 26 – Friday 27 March, 1992
in
Ljubljana, Slovenia, Yugoslavia

The Symposium will consist of a series of invited lectures dealing with the immunological and hormonal changes in pregnancy, the incidence of this condition, natural course of the disease as well as its diagnosis and treatment.

The lectures will be followed by a poster session and oral presentations.

A conference planned for the end of the Symposium is intended to produce guidelines for the diagnosis, treatment and prevention of this rare condition.

For more detailed information please contact:

Symposium Secretariat
Ms. Olga Shrestha
The Institute of Oncology
Zaloska 2, 61105 Ljubljana
Slovenia, Yugoslavia
Tel.: +38 61 327 955
Fax: +38 61 329 177

SEKCIJA ZA RADIOLOGIJU HRVATSKOG LIJEČNIČKOG ZBORA
ODJEL ZA RADIOLOGIJU MEDICINSKOG CENTRA VARAŽDIN

JUBILARNI DESETI ZNANSTVENI SKUP RADIOLOGA HRVATSKE

Varaždin, 4. – 7. prosinca 1991. godine.

DRUGA OBAVIJEST

Teme:

1. Dijagnostička i intervencijska radiologija probavnog sustava
2. Dijagnostička i intervencijska neuroradiologija
3. Slobodne teme

Prijave predavanja i kratke sažetke poslati do 30. 6. 1991. godine na adresu: Medicinski centar, odjel za radiologiju, A. Mihinjača bb, 42000 Varaždin.

Trajanje predavanja do 10 minuta.
Osigurana mogućnost paralelne projekcije standardnih dijapozitiva.
Video projekcije, sistem VHS posebno zatražiti u prijavi rada.

U glavnoj temi: DIJAGNOSTIČKA I INTERVENCIJSKA NEURORADIOLOGIJA organizirat će se TEČAJ IZ KOMPJUTORIZIRANE TOMOGRAFIJE U NEURORADIOLOGIJI. Tečaj je namijenjen liječnicima specijalistima i specijalizantima.
Cijena tečaja uključena je u kotizaciju. Mole se svi zainteresirani da prijavu označe »za tečaj«.
Za sve informacije o tečaju obratiti se na adresu prof. dr. Nada Bešenski, Zavod za radiologiju, KBC Rebro, Kišpatićeva 12, 41000 Zagreb, tel. 233-725 ili 41000 Zagreb, Zvonimirova br. 75, tel. 448-918.

Kotizacija za učesnike u iznosu dinarske protuvrijednosti 60 DM, a za pratioce 30 DM.

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This is to inform the members of pediatric radiology that

THE THIRD SYMPOSIUM OF PEDIATRIC RADIOLOGY OF YUGOSLAVIA

will be held
from **November 6-7, 1991,** in **Belgrade**

Themes of the Symposium:

1. Radiological pathology of the respiratory tract in children
2. Radiologically diagnosed problems of pulmonary diseases
3. Professional problems

Location: The Intitute of Health Protection
of Mothers and Children of SR Serbia
Radoje Dakić 8
11070 New Belgrade

Address for Correspondence:

As above
Attn: Assist. Prof. Pravdoljub Komar, MD, DSc,
Pediatric Radiology

All interested participants are requested to inform Dr. Komar on their intention to take part in the Symposium.

Prof. Nada Grivčeva-Janošević, MD
President,
Department of Pediatric Radiology
Institute of Radiology
Faculty of Medicine
Ul. Vodnjanska 17
91000 Skopje

ALPE–ADRIA RADIATION ONCOLOGY MEETING

NOVEMBER 8–9, 1991 GRAZ / AUSTRIA

Organizer: Division of Radiotherapy, University Medical School

Major Topic: Precision in Radiotherapy and its Impact on Treatment Outcome
Including: Positioning and Immobilisation Aids
Field Localization
Beam-modifying Devices
Treatment Planning
Dose Calculation
Potential for Improvement in Radiotherapy

Congress Language: English

Place of Conference: Lecture hall of the Department of Radiology
Auenbruggerplatz 9, A-8036 GRAZ

Proposed papers with abstracts to: Abteilung für Strahlentherapie
(ALPE-ADRIA Meeting)
Auenbruggerplatz 9
A-8036 GRAZ / AUSTRIA

Deadline: July 31, 1991

Registration: Early: before July 31, 1991
Late: after July 31, 1991

Registration Fee:

before July 31, 1991	after July 31, 1991
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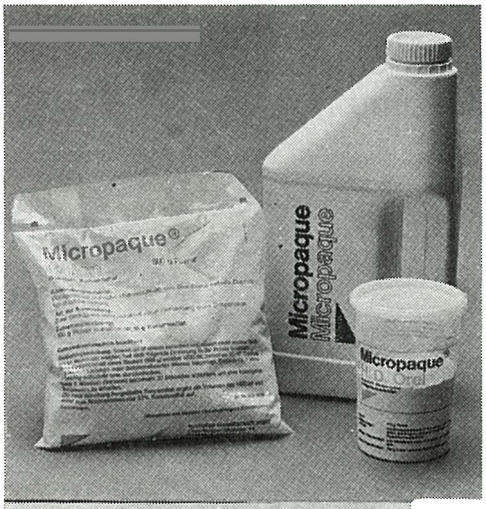

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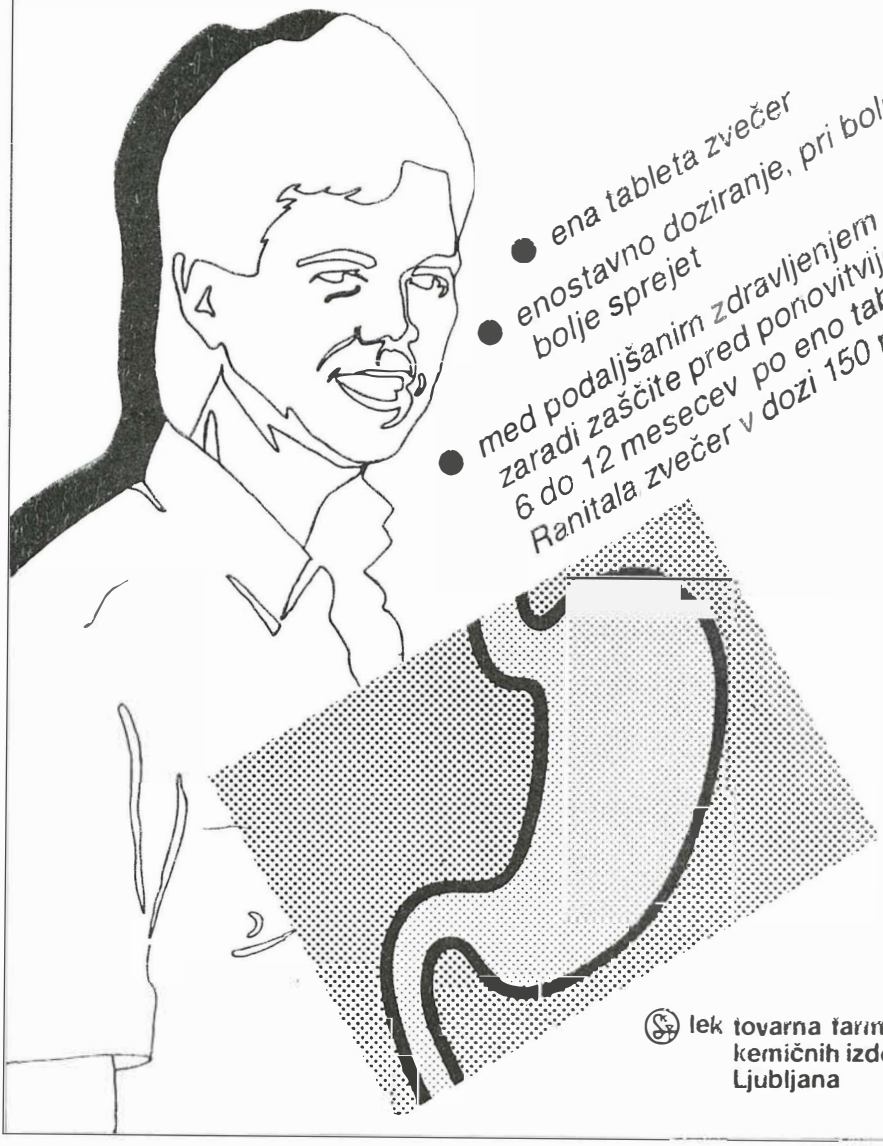

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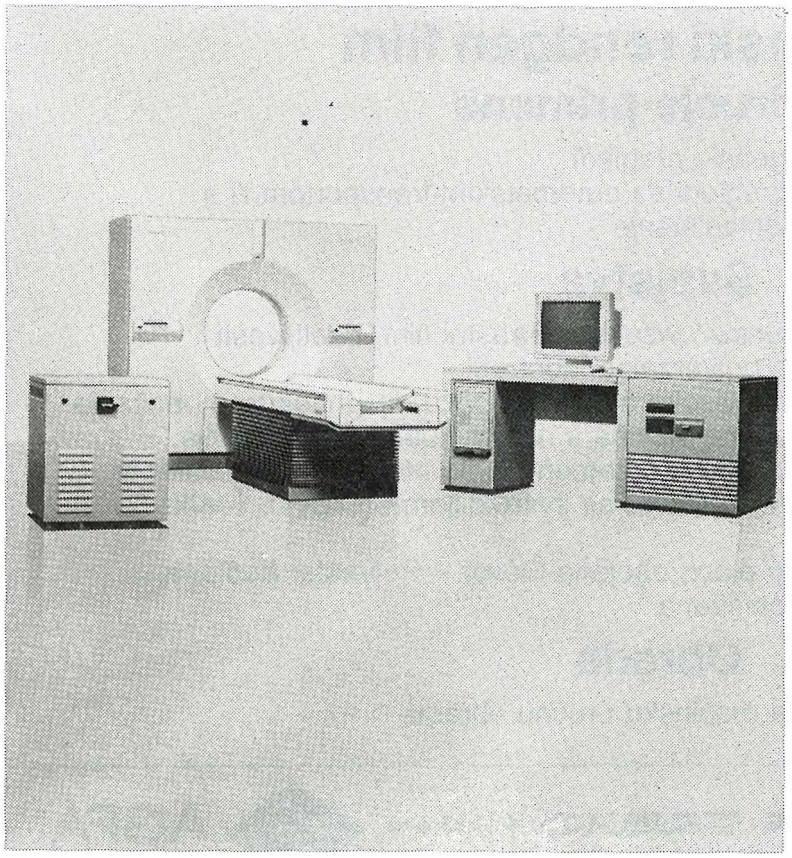

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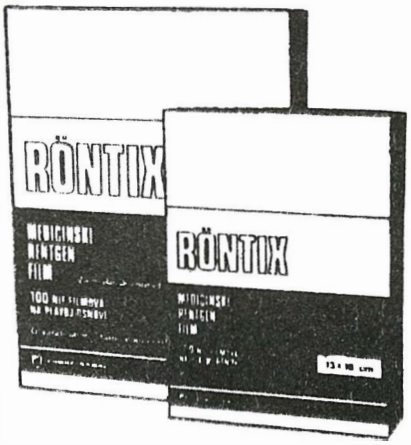

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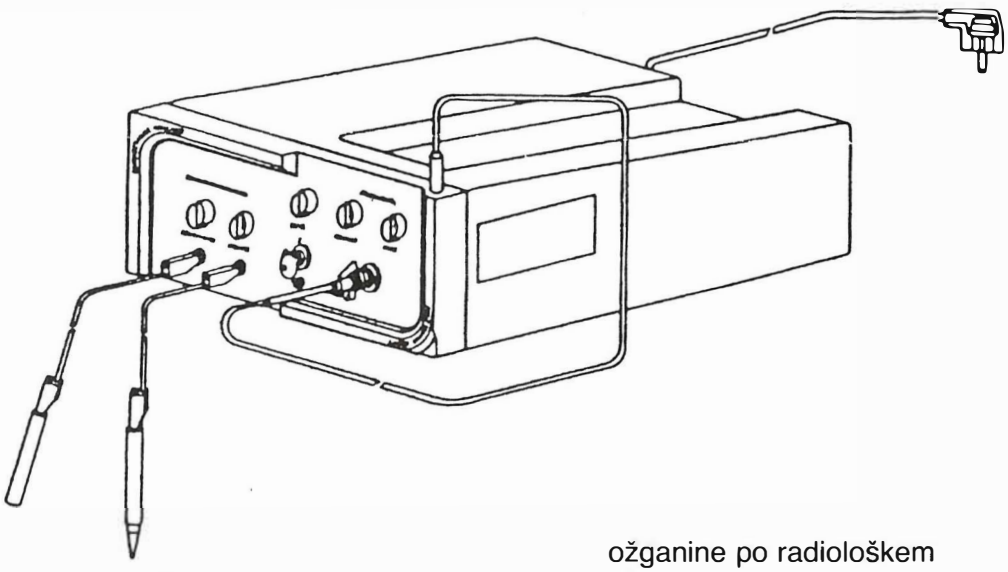

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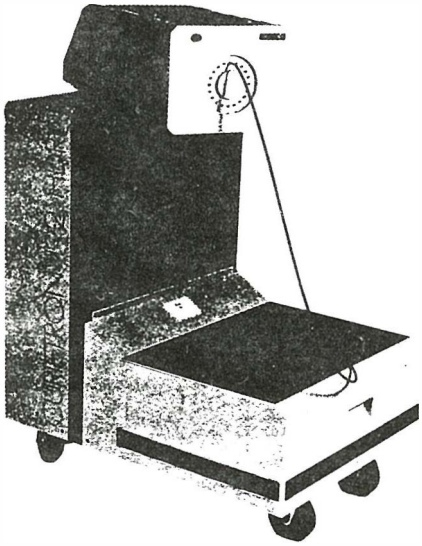

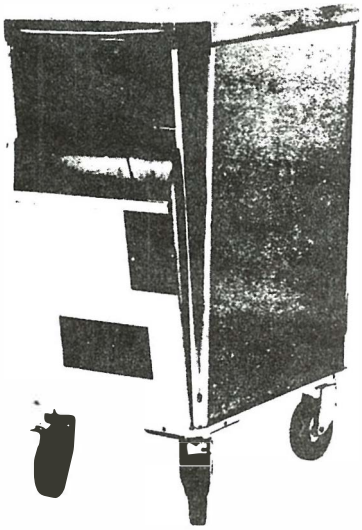

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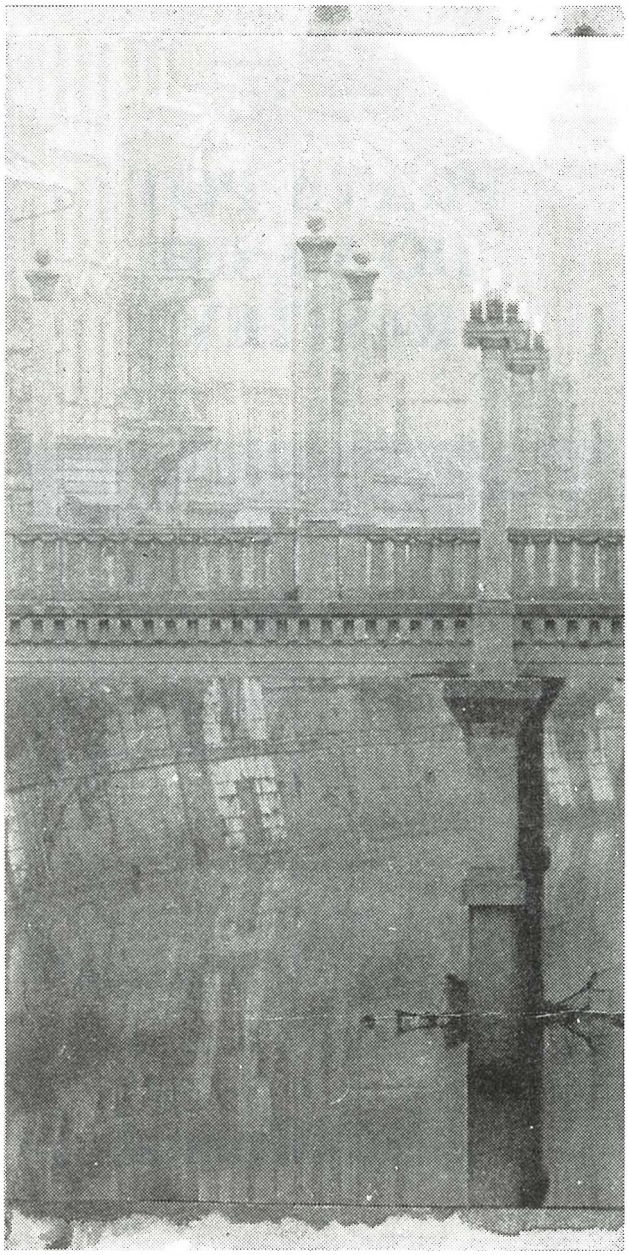

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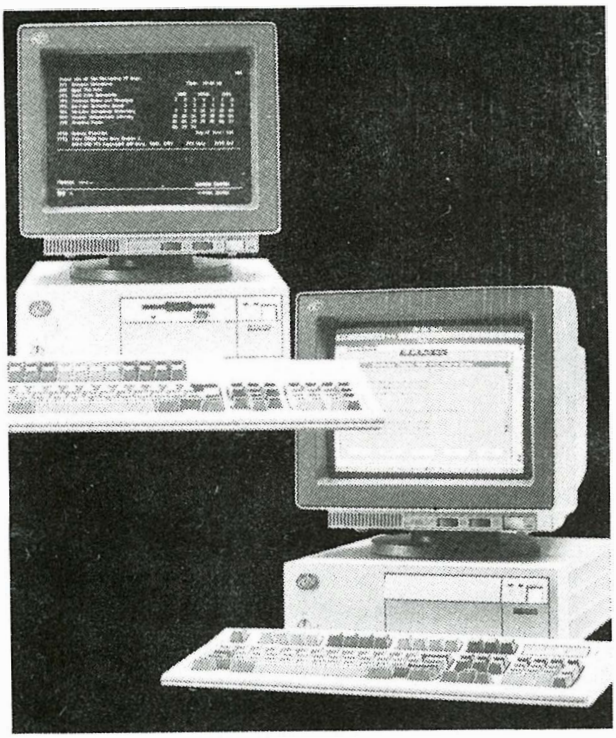

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1. Dent RG, Cole P. In vitro maturation of monocytes in squamous carcinoma of the lung. Br J Cancer 1981; 43:486–95.

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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- Institut za radiologiju i onkologiju UMC-a Sarajevo
- Inštitut za diagnostično in intervencijsko radiologijo, UKC Ljubljana
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— hudih oblik primarnega genitalnega herpesa simplexa
— primarnih in rekurentnih infekcij z varicello zoster pri osebah z normalno in oslabljeno imunostjo
— herpes simplex encefalitisa (fokalnega in difuznega)
— za preporečevanje infekcij s herpesom simplexom pri bolnikih z zelo oslabljenim imunskim sistemom (transplantacije, zdravljenje s citostatiki)

VIROLEX® — mazilo za oči

za zdravljenje

— keratitisa, ki ga povzroča herpes simplex

VIROLEX® — krema

za zdravljenje

— infekcij s herpesom simplex na koži in sluznicah

Podrobnejše informacije in literaturo dobite pri proizvajalcu.

KRKA, tovarna zdravil, n. sol. o., Novo mesto

KRKA

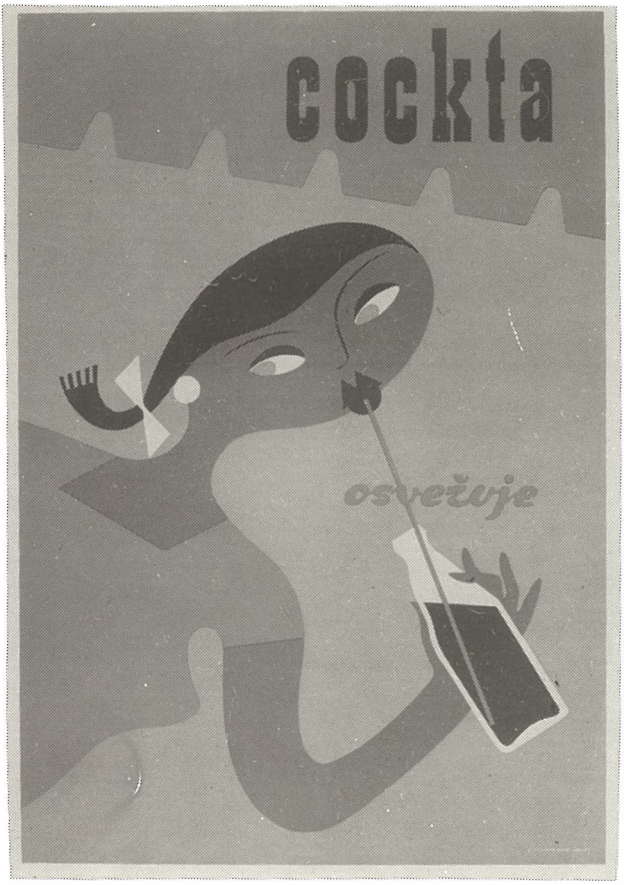
280

industrija pohištva in notranje opreme
nova gorica

65001 nova gorica
jugoslavija
telefon: 065/22 611
telex: 34316 yu meblo

MEBLO

Za opremo vseh bivalnih prostorov
sistemsko pohištvo forma 83, kosovno pohištvo, JOGI vzmetnice, JOGI postelje, spalnice, rustikalno in kolonialno pohištvo, oblazinjeno pohištvo, izdelki iz plastičnih mas (cvetličnjaki, stoli, mize), svetila



Poslovni Sistem

SLOVIN

PHILIPS

avtotehna d.d. PHILIPS

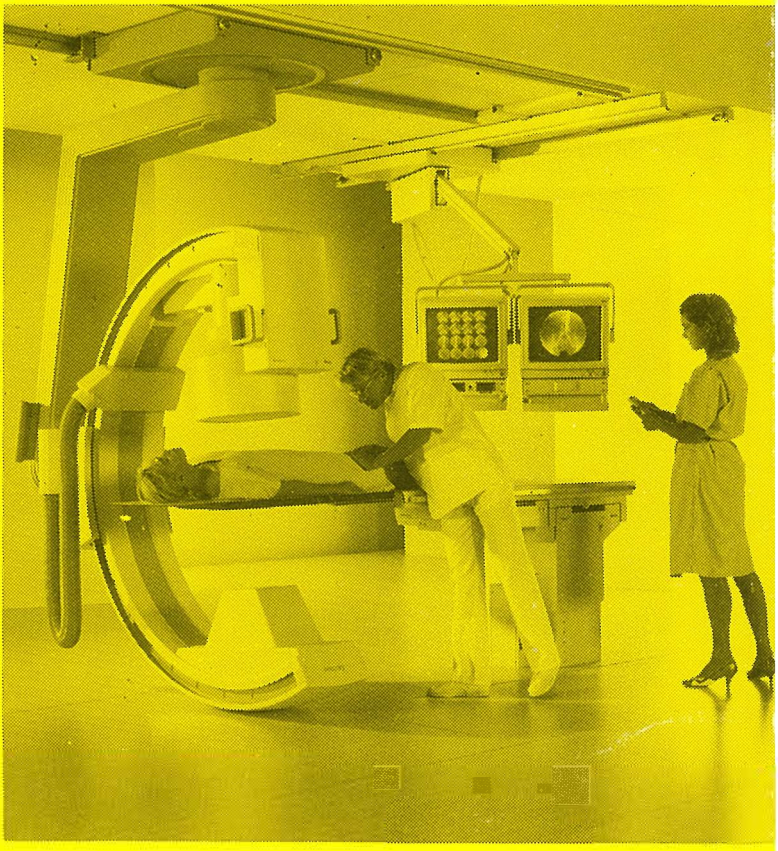
Philips Medical Systems

INTEGRIS 2000

Izredne tehnične latnosti ujete v obliko nagrajeno leta 1990 v Hannovru

Lastnosti:

- popolno prilagodljiv C lok na različne kote preiskovanja
- cerebralna, kardialna, torakalna abdominalna in periferna angiografija
- izpis doze sevanja na posebnem prikazu in opozorilni signal pri prekoračenju
- digitalni slikovni sistem
- shranjevanje slik: na film ali digitalni pomnilnik
- sistem je predviden za priključitev na PACS (Picture Archiving Communication System)



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