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

Phone: + 38 61 120 068 Fax: + 38 61 114 180

Reader for English language **Olga Shrestha** 

Design **Monika Fink-Serša** 

Key words und UDC **Eva Klemenčič** 

Secretaries Milica Harisch Betka Savski

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# Morphological characteristics of renal arteries related to the position and size of the kidney

Dragica Bobinac, Tea Schnurrer, Milivoj Dujmović

Medical Faculty, University of Rijeka, Croatia

The number and diameter of arteries supplying the kidney, and the extension of the main artery to the hilus have been investigated by means of real angiography. We wanted to correlate these data with the size and position of the kidney. It was found that in a certain percentage (in our cases in 14%) the kidneys were irrigated by more than one artery. The diameter of the main artery varied from 5 to 7mm in females and from 6 to 8mm in males. The diameter accessory arteries was markedly smaller, ranging from 3.5 to 4mm. The measured length and width of the kidneys showed that these were smaller in females than in males. As a rule, the right kidney was smaller that the left one. There was no correlation established between the main artery diameter and the size of the corresponding kidney, indicating that the diameter did not depend on the organ size. Generally, the course of the arteries was tortuous, extending caudally at first, and then making a bend with downward convexity, and ending with the ascending segment approximately in the horizontal plane. This segment was also found to correspond to a normal anatomical position of the kidney, and such a course was invariably associated with the mentioned position.

Key words: kidney anatomy and histology; renal artery radiography, renal size, renal position, renal artery diameter

#### Introduction

According to the data reported in literature, morphological characteristics of the renal arteries and the kidney are independent entities that cannot be correlated to each other. Thus, the data on the number of renal arteries, the level of their arising from the aorta and their further progression are most frequently associa-

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ted with segmental distribution of the renal parenchyma.<sup>1-5</sup> As for the kidneys, there are reports on their size and skeletopic relations pointing to the position of the kidney.<sup>6-9</sup> The purpose of this study was to establish whether there was a correlation between the number and diameter of renal arteries, i.e. the transverse section assessed from the diameter and the renal sectional area regarding variable diameters and the number of these blood vessels, and the organ size showing numerous variations.<sup>10</sup> Furthermore, we were interested in the relation between the direction and the way of renal artery extension, and the kidney position because of individual differences related to that;

Correspondence to: Assist. Prof. Dragica Bobinac, MD, Medical Faculty, University of Rijeka, Olge Ban 20, 51000 Rijeka, Croatia.

as reported in literature, kidney position may range from cranial vertebral level, or caudally from the common skeletopy of the right and left kidney. We wanted to find out whether, and in what way, the extension direction adjusted to the kidney placed somewhat higher or lower from the ordinary position, or whether all the arteries would behave in the same way in the case of congenital organ position.

#### Material and methods

Radiograms of patients treated at the Clinic of Radiology, Clinical Center in Rijeka were used in our study. They were taken during renal angiography, imaging the kidneys with their arteries and aorta along with other visceral and parietal branches, and the terminal ramification of the aorta to common lateral arteries.

From a great number of renal angiograms surveyed, those with neither signs of vascular changes nor renal parenchyma alterations were selected. Thus a sample of 50 patients, 30 males and 20 females, with kidneys and renal arteries within the physiological range was obtained.

Radiograms were taken in a standard a.p. projection with focus-film distance of 75 cm.

The number of renal arteries of the right and left kidney, respective of the fact whether the kidney had a single artery or there were also accessory arteries present, was assessed on Xray images of the arterial phase of renal angiography. Afterwards, the arterial diameter was measured at 1 cm distance from the arising point from the aorta. Mutual relation between the height of the left and right renal arteries arising points from the aorta was also observed. The angles indicating the course, i. e. the ordinary arterial extension, were measured on the same radiogram:

a) the angle between the aorta extension direction at the height of the arising point of the renal artery and the direction of the initial part of the same artery;

b) the angle between the aorta direction at the height of the renal artery arising point and the line connecting the arising point with the point of the first ramification of the same artery. This connection line represents the ordinary arterial direction.

Renal length and width were measured during the nephrographic phase because of clearly delineated organ shadow.

The renal length was measured as the distance between the most projecting polar points. Because of the suprarenal gland position above the upper pole of the kidney, being in close relation with it, we had to define the upper pole of the kidney carefully.

The renal width was measured at its widest part perpendicularly to its length. Because of its anatomical position, the kidney was slightly rotated in the frontal plane, facing ventrally and laterally with its anterior surface, and the organ width measured on radiogram was somewhat lesser than its real size. The frontal renal sectional area was calculated from known values of length and width using the formula for ellipse area evaluation. At the same time, the position of the inferior pole of the right kidney was marked in relation to the left one, and to the lateral ridge if the inferior pole was sufficiently low to cross it.

Finally, the longitudinal sectional area of the kidney was correlated with the sectional area of the artery diameter, or arteries in the case of accessory vessels presence. Cross-sectional area of the artery was obtained by means of the formula for circular area calculation from a known diameter, i. e. the diameter of the artery.

The data were statistically analysed.

#### Results

The main renal artery varies according to the level of the arising point from the aorta, the way of ramification and the diameter of accessory arteries present in a certain percentage of the kidneys. The accessory arteries also arise from the aorta, most frequently directly entering the parenchyma in the polar area, being of a smaller diameter. Of 100 investigated kidneys, 14 (14%) were found to have accessory vessels present, mostly unilaterally, i.e. either on the right or on the left, except in two cases with two arteries on each side, and another case with two arteries on the right and three arteries on the left (Table 1).

The diameter of the main renal artery, is significantly greater than the accessory artery diameter, if the latter is present. The results of measurements were grouped separately for the right and left arteries, as well as according to sex in order to establish possible correlation between the observed parameters. Thus the average value of the main renal artery diameter, measured at the distance of 1cm from the arising point, was found to be somewhat lesser in females, the corresponding values being  $0.62 \text{ cm} (\pm 0.08)$  for the right and  $0.65 (\pm 0.09)$ for the left vs 0.69 cm ( $\pm$  0.10) for the right and  $0.70 \,\mathrm{cm} \,(\pm 0.12)$  for the left in males (Table 2). Comparing the right and left artery diameters, the left arteries were found to have greater diameters than the right ones in most cases, or both were of the same diameter. Thus a greater diameter of the right artery was most uncommon. Therefore, the average values of the right and left arteries display their real relationship to each other.

The average value of accessory artery diameter is markedly lower in comparison with that of the main artery, being also slightly lower in females than in males, the respective values being  $0.35 \text{ cm} (\pm 0.07)$  bilaterally in the former vs 0.44 cm ( $\pm$  0.11) for the right and 0.35 cm ( $\pm$  0.14) for the left in the latter (Table 2).

The renal artery extends in its tortuous course laterally to the kidney. Its course was presented by measuring the angle pointing to the initial arterial course and the angle displaying the course of the distal part of the artery. The obtuse angle obtained by measuring the angle between the aorta and the initial part of the artery indicates a descending course of the initial segment of both, the right and the left artery, showing a steeper caudal arterial extension in females than in males. Thus the average values of this angle were  $121.6^{\circ}$  (± 19.76) for the right and  $118.7^{\circ}$  (± 10.76) for the left in females (Figure 1) vs  $111.1^{\circ}$  (±20.09) for the right and  $114.4^{\circ}$  (±11.62) for the left in males (Figure 2).

The angle presenting the course of the distal part of the artery, measured between the aorta and the line connecting the arising and the ramification points, is lesser than the former one, getting close to the horizontal plane. The average values of these angles are  $113.35^{\circ}$ ( $\pm 23.23$ ) for the right and  $90.1^{\circ}$  ( $\pm 20.16$ ) for the left in females vs  $97.8^{\circ}$  ( $\pm 18.3$ ) for the right and  $93.5^{\circ}$  ( $\pm 20.03$ ) for the left in males (Figures 3, 4). Consequently, the renal artery has a descending course in its initial part, afterwards making a bend with caudal convexity since the

Table 1. Total number of renal arteries on the right and on the left.

Number	1 Artery		2 Arter	2 Arteries		rteries
of arteries	Right	Left	Right	Left	Right	Left
100	43	43	7	6	0	1
	86 (80	5%)	13 (13 %	%)	1 (	(1%)

Table 2. Average diameter values of the main and the accessory, renal arteries in females and males (cm).

	Right		Left		Right		Left	
	Main	Accessory	Main	Accessory	Main	Accessory	Main	Accessory
MEAN (cm)	0.62	0.35	0.65	0.35	0.69	0.44	0.70	0.35
STD DEV	0.08	0.07	0.09	0.07	0.10	0.11	0.12	0.14
STD ERR	0.018	0.05	0.02	0.05	0.02	0.05	0.02	0.07
MAX.	0.07	0.40	0.80	0.40	0.90	0.60	0.90	0.50
MIN.	0.50	0.30	0.50	0.30	0.50	0.30	0.40	0.20

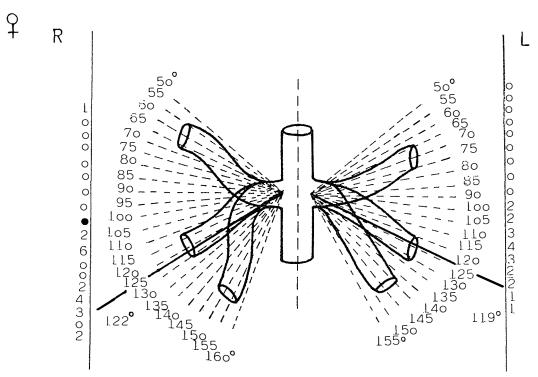


Figure 1. Angles between the aortic direction. at the site of the arising point of the renal artery and the direction of the initial part of the renal artery in females.

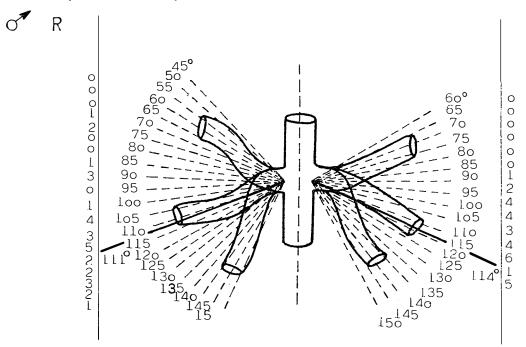


Figure 2. Angles between the aortic direction at the site of the arising point of the renal artery and the direction of the initial part of the renal artery in males.

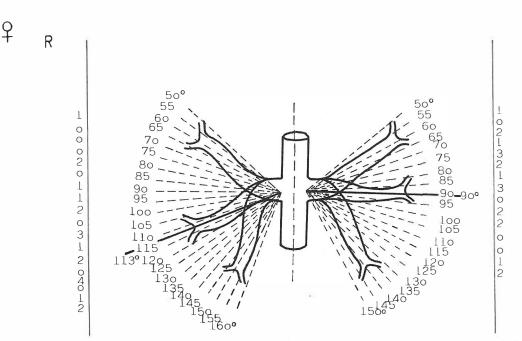


Figure 3. Angles between the aortic direction at the site of the arising point of the renal artery and the lines connecting the arising point of the renal artery with the first ramification point in females.

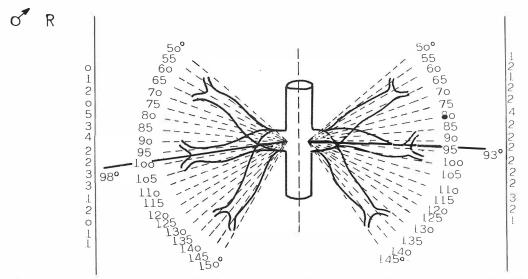


Figure 4. Angles between the aortic direction at the site of the arising point of the renal artery and the lines connecting the arising point of the renals artery with the first ramification point in males.

distal part of the blood vessel has an ascending direction toward the site of ramification. Branches extend dissimilarly from the ramification point.

Renal length and width were measured during the nephrographic phase of renal angiography. The mean values obtained in females were 12.7 cm  $(\pm 0.80) \times 6.4$  cm  $(\pm 1.09)$  for the right and 13.2 cm  $(\pm 1.13) \times 6.7$  cm  $(\pm 0.77)$  for the left. The kidneys in males were larger than in females, their mean values being 13.2 cm  $(\pm 1.31) \times 6.7$  cm  $(\pm 0.90)$  for the right kidney

-								
	Right		Left		Right		Left	
	Main	Accessory	Main	Accessory	Main	Accessory	Main	Accessory
MEAN (cm)	12.70	6.46	13.26	6.70	13.26	6.74	13.44	7.52
STD DEV	0.88	1.10	1.14	0.77	1.31	0.90	1.32	0.63
STD ERR	0.19	0.24	0.25	0.17	0.24	0.16	0.24	0.11
MAX.	14.80	9.90	16.40	8.20	17.40	9.60	16.30	8.40
MIN.	11.50	5.10	12.10	5.30	11.20	5.30	11.30	6.00

Table 3. Average length and width of the kidneys in females and males (cm).

and  $13.4 \text{ cm} (\pm 1.32) \times 7.5 \text{ cm} (\pm 0.63)$  for the left one (Table 3). Here, it needs to be emphasized that the left kidneys had greater lengths and widths than the right ones in a majority of cases.

Besides numerically, the results were also graphically presented in order to enable a simple comparison of the studied parameters of the same kidneys. To compare the diameters of the main and accessory blood vessels with the size of the corresponding kidney, cross-sectional areas of all arteries supplying the kidney were calculated and the longitudinal sectional area of the kidney was assessed from its length and width. The results were separately presented for the right and the left kidneys, according to sex (Figures 5, 6, 7, 8). Graphic presentation of cross-sectional areas of all renal blood vessels clearly showed difference between the diameters of the right and left side, though these were found to be the same in one part of cases. The average values pointed out a slightly greater diameter of the left artery, which was expected and therefore could not be regarded as a relevant indicator, considering that the left kidney is as a rule greater than the right one. On the

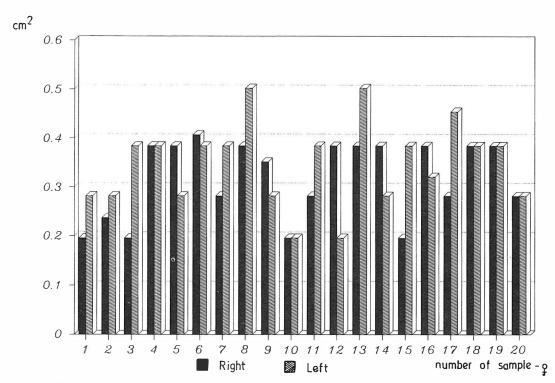


Figure 5. Cross-sectional area of the main and accessory renal arteries on the right and the left side in females  $(cm^2)$ .

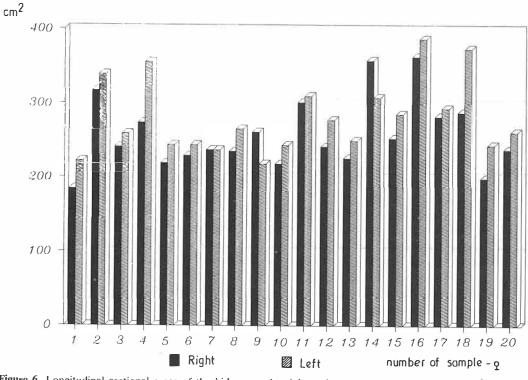


Figure 6. Longitudinal sectional areas of the kidney on the right and on the left side in females (cm<sup>2</sup>).

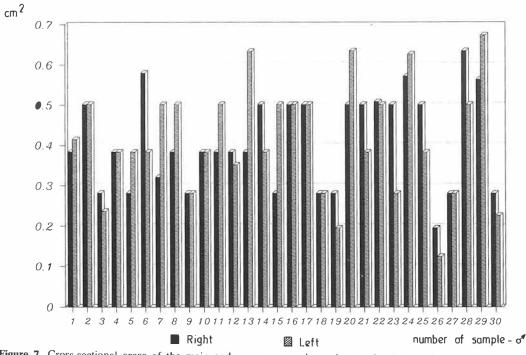


Figure 7. Cross-sectional areas of the main and accessory renal arteries on the right and on the left side in males  $(cm^2)$ .

other hand, the diameters of renal blood vessels in males were greater than those in females, and the range within measured diameters was also greater (Figures 5, 7). On the contrary, longitudinal sectional areas of the kidney evidently showed the left kidneys to be generally larger than the right ones in both sexes (Figures 6, 8). No correlation between them was observed when the arterial diameter was compared with the size of the corresponding kidney. If one or more accessory arteries were found together with the main artery, this increased the total cross-sectional area, though it did not imply any correlation with the organ size. This is best illustrated by the case of a female patient (kidney number 6, Figure 6) who had the right kidney smaller than the left one, and presented with one accessory artery besides the main one, and a greater transverse section on the right than on the left. Another example is a female patient with the left kidney larger than the right one, having one accessory artery, but their total cross-sectional area being smaller than that of the single right artery.

Finally, in order to establish the kidney's position, the projection of the inferior renal pole to the spine and relationships between the inferior poles of the right and left kidneys were determined. The results showed the inferior pole of the right kidney to be mostly projected at the level of L3/L4 discus, and the left one at the level of the medial third of L3 in both sexes. A lesser number of kidneys, not projected at this level, were positioned at the height range of one vertebra below or above the aforementioned finding. Consequently, the right kidney is situated lower than the left one. However, when mutual relations of the inferior renal poles were correlated by sex, lower position of the right kidney in comparison with the left one was established in 95% of females and 63% of males. In the remaining cases both kidneys were situated mostly at the same level. whereas lower position of the left kidney infe-

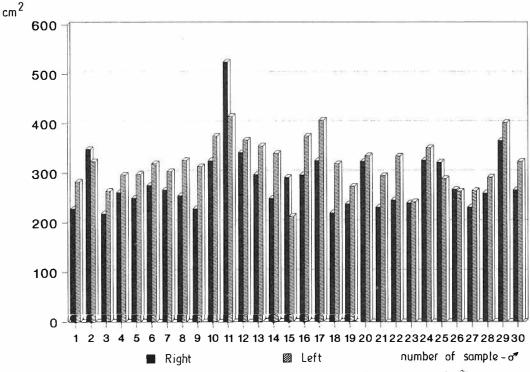


Figure 8. Longitudinal sectional areas of the kidney on the right and the left side in males (cm<sup>2</sup>).

rior pole was observed in the least number of cases.

#### Discussion

The diameter and extension direction of the right and left renal arteries were studied on radiograms of the arterial phase of renal angiography. Width and length of the right and left kidneys were measured during the nephrographic phase when the kidneys were clearly displayed. The obtained results were also grouped by sex.

According to our findings, kidneys were supplied by one renal artery in 86% of cases, whereas in the remaining 14% one or two accessory arteries were present mostly unilaterally either on the left or on the right at an equal percentage. Bilateral accessory arteries were found in two cases only. There was no difference in the frequency of their left/right position by sex.

The obtained percentage presenting the occurrence of accessory arteries supplying the kidney is somewhat lower than the results of most authors who report 23% to 27% of kidneys with accessory arteries.<sup>4, 5, 11</sup> Data of other authors prove the occurrence of accessory arteries to be greatly varying, ranging from only  $5.3\%^{1, 2}$  to even  $42.5\%^4$  of kidneys with more than one artery. Our results, as well as those of all other authors, show the percentage of kidneys with two or more accessory arteries to be very low. The greater the number of these arteries is, the lower the percentage of occurrence.

The average values of renal artery diameters are presented separately for the right and for the left side, and according to sex. Our data for females show slightly lower values in comparison with males, i. e.  $0.62 \text{ cm} (\pm 0.08)$  for the right and  $0.65 \text{ cm} (\pm 0.09)$  for the left in the former vs  $0.69 \text{ cm} (\pm 0.10)$  for the right and  $0.70 \text{ cm} (\pm 0.12)$  for the left in the latter group. The bibliographical data have not been cited in pursuit of our systematization, but most authors report a uniform diameter of the main renal artery of 7 mm.<sup>13, 14</sup> Measuring diameters, Merklin<sup>11</sup> and Kus<sup>15</sup> obtained the average value of 5.5mm which was markedly lower than our results, representing almost the lowest values within the ranger of our measurements (5-9 mm).

Present accessory arteries are easily distinguished from the main artery because of a smaller diameter. In females the diameter is  $0.35 \text{ cm} (\pm 0.07)$  for both the right and the left side, whereas in males the relevant values for the right side are insignificantly greater, being  $0.44 \text{ cm} (\pm 0.11)$  for the right and  $0.35 \text{ cm} (\pm 0.14)$  for the left side. Otherwise, diameter varies from 0.2 to 0.6 cm in all accessory arteries. Consequently, it is roughly equal for both the right and the left, showing no difference according to sex. Average values of accessory artery diameters have not been found in the literature, however, their diameter range from 1 to 6 mm is reported.<sup>11</sup>

There is no rule as to the kidney size with respect to the side (left/right) or sex, and therefore mean values of renal length and width almost unexceptionally mean that the left kidney is of a greater length an width than the right one, so in males as well as in females. The obtained results correspond to those of Moell,<sup>7</sup> and similar results have been reported by Merklin<sup>11</sup> with a distinction that the left kidney is longer and narrower than the right one.

If we study the position of the kidney in relation to the spine, the right kidney is generally situated lower that the left one projecting its inferior pole at the level of L3/L4 discus, whereas the inferior pole of the left kidney projects at the level of the medial third of L3. Data found in the literature are rather inaccurate. Mainly, projections of the right kidney inferior pole at the L3 level, and the left one at the L2 level are reported. More precise data about the right kidney inferior pole projection at the L3 level, and the left one at the level of lower edge of L2/L3 discus can be found in Kus's<sup>15</sup> paper only. The results presenting mutual relation of inferior pole in both kidneys are in complete agreement with data from the literature.9, 16

Studies of main renal arteries using corrosion

preparations or a radiologic technique<sup>5</sup> show the branches of the renal artery to supply their own part of parenchyma each, corresponding to a segmental division of the same. In the case of the presence of accessory arteries they independently supply a part of parenchyma corresponding to one segment. Thus accessory arteries prove to be functionally indispensable by supplying the organ together with the main artery. Their smaller diameter relating to the main artery has been justified for they supply a smaller part. Furthermore, in the presence of an accessory artery, the main one is found to be of a smaller diameter, so that a total surface corresponds to a certain average value. No correlation was established between the cross sectional area of the main artery and the kidney surface, despite somewhat greater average values of the left artery diameter than the right one, which could point out a correlation with greater surface of the left kidney in comparison with the right one. If accessory arteries are also present in the kidney, their diameter should be summed up without changing mutual relations between the diameter of renal arteries and the kidney size. Consequently, the difference in the diameter of the main artery and the accessory ones, if present, has not been conditioned by the size of the kidney.

The course of the main renal artery from the aorta up to the ramification point before the hilus has been presented by measuring angles between the aorta and the initial part of the artery, and between the aorta and its ramification point. According to our results, the main artery is not extending in straight lateral direction as reported in anatomic textbooks, but instead having a rather tortuous lateral course. The initial arterial direction is descending, and afterwards making a convexity turn downwards. Hence, the distal arterial part has an ascending course up to the ramification point. The ramification point approaches the horizontal plane, which means that the angle between the aorta and the ramification site is approximately 90°. The initial course of the right artery is generally more steep than the left one, thus being in agreement with the data form literature stating the right kidney to be lower than the left one.<sup>6</sup> Except, compared to the data of other authors, the right artery arises at a higher level than the left one in the largest percentage of cases, which further proves its steeper course.<sup>1, 11, 17</sup>

The branches extend in various directions, i.e. ascending and descending from the ramification site. But it could also be seen that all branches of the renal artery extended downwards in some kidneys with the arterial stem of completely normal course. By having determined the skeletopic relation of the inferior renal pole against the spine, we established its position at the lower limit of normal finding which corresponds to the medial third of L4 for the right kidney and L3/L4 discus for the left one. The direction of renal artery branches in some other kidneys, the inferior poles of which were also projected lower than in most of them, was completely normal. Therefore, a descending direction of all branches of the renal artery could possibly be regarded as a sign of initial lowering of the kidney, or just a change of the position as such is possible. Further investigation should establish the degree of reliability of this sign with reference to these hypotheses.

#### Conclusion

The kidney is supplied by a single renal artery arising from the aorta, which is branched and its branches enter the kidney at the hilus in 80% of cases. In the remaining 14% of cases one or even two arteries along with the main one could be seen entering the kidney, but directly into the parenchyma past the hilus; they are called the accessory arteries.

The average value of the main renal artery diameter ranges from 6.2 to 7 mm, depending on the side and sex. Females present with a somewhat smaller diameter, their values being between 5–7 mm, for the distinction from males whose values are in the range between 6 and 8 mm. The diameter of accessory arteries is markedly smaller then that of the main artery, ranging from 3.5 to 4 mm.

The renal artery has a tortuous course, des-

cending in its initial part, and then proceeding in ascending distal direction up to the ramification point where it makes a bend with downward convexity. Branches show ascending, horizontal and descending courses after the ramification point, entering the renal parenchyma at the hilus.

The left kidney is longer and wider than the right one in both males and females. The position of the renal inferior pole in both sexes is at the level of L3/L4 discus in the right kidney, and at the level of the medial third of L3 in the left one. These data are in agreement with the finding that the right kidney is situated lower than the left one.

There was no correlation betwen the parameters comparing the values of the cross-sectional area of the main and accessory arteries, if present, with the kidney surface. Hence we have concluded that the different values of arterial diameter are not conditioned by various size of the kidney.

Comparing the anatomic position of the kidney, and the obtained data on the ordinary course of the renal artery, we have concluded that there is direct mutual correlation between these two parameteres. Therefore a change in the direction of artery extension would indicate a position change of the kidney itself.

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## Rare localizations of Crohn's disease in the gastrointestinal tract

Marija Frković, Renata Vučković, Ante Mandić

Clinical Hospital Center Rebro, Department of Radiology, Zagreb, Croatia

Crohn's disease can affect the whole gastrointestinal tract, although the most common site involved is terminal small bowel. The esophagus, stomach, duodenum and proximal small bowel are rarely affected. Such cases are described as rare localizations of Crohn's disease. This study presents a retrospective analysis of 24 (22,6%) patients with uncommon sites of Crohn's disease, identified in the group of 106 patients in whom the diagnosis of Crohn's disease was made during the period from 1980–1990.

Key words: gastraointestinal diseases-diagnosis; Crohn disease

#### Introduction

Although terminal small bowel is the most common site involved in Crohn's disease, it can affect any part of the gastrointestinal tract from the mouth to anus.<sup>1,2,3,4,5</sup> The esophagus, stomach, duodenum and proximal small bowel are rare localizations of Crohn's disease with the incidence of 0.5-7 %.<sup>6,7,8</sup>

In 1950 Comfort et al.<sup>9</sup> reported on five patients with granulomatous disease of the duodenum and small bowel.

Three years later Martin et al.<sup>10</sup> presented two patients with Crohn's disease of the stomach. At the same time, in a number of studies, patients with "regional esophagitis" were reported.<sup>11, 12</sup>

Considering a small number of patients with

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Crohn's disease of the upper gastrointestinal tract, and the importance of double contrast examinations as diagnostic procedures (in Crohn's disease), the specific radiologic signs, as well as the possibilities of radiologic diagnostic procedures in Crohn's disease of the esophagus, stomach, duodenum and proximal small bowel are described in our study.

#### **Patients and methods**

From 1980–1990, the diagnosis of gastrointestinal Crohn's disease, using double contrast examinations of the gastrointestinal tract, was made in 106 patients at the Department of Radiology Clinical Hospital Center Rebro.

Each patient underwent routine double contrast examination of the whole gastrointestinal tract.

Barium meal and *follow-through* examinations were obtained with 200 ml barium given orally. The large bowel was examined by double contrast barium enema.

Corespondence to: Marija Frković MD, Clinical Hospital Rebro, Department of Radiology, Kišpatićeva 12, 41000 Zagreb, Croatia.

The diagnosis of Crohn's disease was made on the basis of the characteristic radiologic signs.

The early, non-stenotic stage of the disease is characterized by aphthous ulcers as the earliest radiologic signs, thickened folds, big ulcers and cobblestoning.

The appearance of fibrosis and scarring in the later stenotic stage results in progressive obstruction of the esophages, stomach and/or duodenum and proximal small bowel. Radiologic signs of Crohn's disease are therefore the same in the proximal as well as in the distal parts of the gastrointestinal tract.

In 24 (22,6%) patients we identified gastrointestinal Crohn's disease in localizations considered as rare.

#### Results

The distribution of patients with rare localizations of Crohn's disease in the gastrointestinal tract is presented in Table 1. All patients underwent endoscopic examination and three of them

Table 1. Distribution of patients with rare le	ocalizations
of Crohn's disease in the gastrointestinal	tract.

Rare localizations	No. of patients	Affected ileocecal segment	Correctness of rtg diagnosis
esophagus	3 (12,5%)	2	2
stomach	4 (16,7%)	4	3
duodenum	7 (29,1%)	7	7
jejunum	10 (41,7%)	8	8
Total	24 (100%)	21 (87,5%)	20 (83,3%)

were surgically treated owing to the complications in the distal segments of the gastrointestinal tract. In all our patients the pathohistologic analysis confirmed Crohn's disease.

In statistical analysis the standard error of proportion calculated by formula

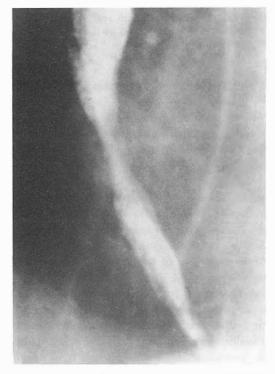
$$s_p = \sqrt{\frac{p \cdot q}{N}}$$

equals to 0.0193. That means that the obtained result is statistically important at a better level

than possible error of 95%. In  $\pm 2$ , standard errors ( $\pm 0.0386$ ) are 95% of the results, and in  $\pm 3$ , standard errors ( $\pm 0.0579$ ) are 98% of possible results (i. e. between 16.8% and 28.4%).

#### Discussion

Double contrast examination of the gastrointestinal tract offers significant possibilities in identifying early changes in the gastrointestinal tract caused by Crohn's disease.<sup>13, 14</sup> The relative accuracy of the diagnosis of Crohn's disease in rare localizations by double contrast examination of the gastrointestinal tract is 83.3%; this is encouraging, but also requires caution since even though the radiologic signs of the disease in the proximal segments of the gastrointestinal tract are specific, in the final diagnostic conclusion we must consider clinical symptoms as well



**Figure 1.** Crohn's disease of the esophagus-edematous folds with submocous ulcerations in the distal portion of the esophagus.



**Figure 2.** Thickened folds with aphthous ulcerations of the body and antral region of the stomach. The duodenum is also affected.

as pathologic changes in the distal segments of the gastrointestinal tract.

In most of our patients the terminal ileum and/or large bowel are changed, which is evident from our statistically analysed results (87.5%).

Among our three patients with Crohn's disease of the esophagus (Figure 1) we had certain diagnostic problems with an 18 month old infant. In this patient at the site where the middle third of the esophagus passes into the distal third, narrowing of the lumen and a shallow ulcer were found, so the radiologic diagnosis was congenital structure. This could not be evaluated endoscopically. The infant underwent surgery and pathohistologic finding confirmed granulomatous reaction. In other segments of the gastrointestinal tract etiologically identical changes were not found.

Crohn's disease of the stomach (Figure 2) is almost always confined to the antrum or antrum

and body,<sup>2,6,8,15</sup> and often to the duodenum.<sup>2,16</sup> In all our patients specific changes were found in the medial part of the body of the stomach, as well as in the antral region. In three patients the duodenum was also involved.

In one patient in whom changes were confined only to the stomach the radiologic diagnosis was carcinoma (Figure 3). The pathohistological examination after surgery confirmed the diagnosis of Crohn's disease.

This experience, as well as data from the literature confirm the opinion that sometimes it is almost impossible to differentiate scirrhous carcinoma from gastric Crohn's disease.

Differential diagnostic possibilities of roentgenographic manifestations must include: corrosive gastritis, erosive gastritis, benign hyperplasia<sup>17</sup> lymphoma and other granulomatous diseases.<sup>2,6,8,10</sup>

According to Nelson,<sup>8</sup> changes which in continuity affect the central region, pilorus and

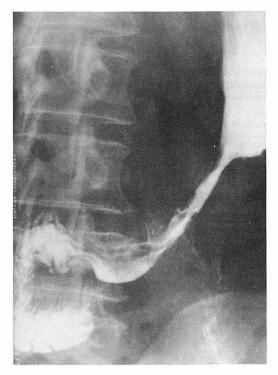


Figure 3. Stenotic phase of Crohn's disease of the stomach is difficult to differentiate from scirrhous carcinoma of the stomach.



Figure 4. Crohn's disease of the proximal jejunal loops.

proximal duodenum are similar to the conditions of postoperative Billroth I – pseudopost Billroth I, and if they are found in non-operated patients they suggest granulomatous disease.

Crohn's disease confined only to the duodenum is more frequent that Crohn's disease confined only to the stomach.<sup>16</sup>

Aphthous ulcers, which are one of the first signs also in duodenal Crohn's disease, are more difficult to demonstrate than in the stomach because of duodenal folds.<sup>19</sup> In many cases these ulcers may be identical to peptic ulcers, but the presence of changes in the antral region of the stomach and in the distal parts of the duodenum will confirm the correct diagnosis.<sup>19</sup>

In the descending parts of the duodenum as well as in other parts of the gastrointestinal tract both ulcerations and oedematous folds can be found. In later stages the narrowing of the lumen, if present in the second or third part of the duodenum, can result in megaduodenum.<sup>15</sup> As the narrowing of the lumen is asymmetric in uninvolved segments the crypts and pouches are frequently demonstrated and they look like diverticula – pseudodiverticula.<sup>5,8</sup>

In differential diagnosis pancreatitis which can occur in these patients most commonly mimics the changes of regional enteritis.<sup>15</sup>

Jejunal Crohn's disease appears in 4-10% of the patients with characteristic changes of terminal ileum<sup>21,22</sup> which can also be seen from our results (9.4%). Characteristic radiologic signs as thickened folds, ulcerations and narrowing of the lumen are present. The separation of rigid loops fixed to mesenteric border, leads to the ballooning of the antimesenteric border. This is seen in approximately 8% of patients.<sup>22</sup>

It is sometimes difficult to diagnose jejunal Crohn's disease correctly, especially when the characteristic changes are not evident in the terminal ileum. Inflammation of other ethiology, metastases, lymphoma, carcinoid and mesenteric processes can be manifested similarly.<sup>23</sup>

In our two patients who did not have specific changes in the terminal ileum, malignant lymphoma was diagnosed. In the later stage of the disease one of these patients underwent surgery due to complications of Crohn's disease. The pathohistologic finding was Crohn's disease.

In other patients, changes in the terminal ileum specific for Crohn's disease were detected on follow-up examination.

Considering the above stated facts, we can conclude that Crohn's disease in rare localizations found in 24 (22%) patients is not so rare.<sup>6,7,8</sup>

Statistical analysis of the obtained results proved their significance, and therefore we believe that our findings can be regarded as conclusive rather than accidental. This at the same time confirms the part of the definition of the disease according to which Crohn's disease affects the intestinal tract from the mouth to anus.

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# Pulsed-wave and color-doppler in the assessment of native kidneys with urinary tract obstruction

### Boris Brkljačić, Ivan Drinković, Dragica Soldo, Vinko Vidjak, Drago Odak, Andrija Hebrang

Ultrasonic Centre, Clinical Department of Radiology, Medical Faculty of Zagreb, University Hospital »Merkur«

We measured average resistance indices (RI) in intrarenal arteries in 48 kidneys of 24 healthy volunteers, without known renal impairment, and in 15 patients with unilateral urinary tract obstruction, comparing indices in obstructed and contralateral unobstructed kidneys. Average RI in kidneys of healthy volunteers was  $0.59 \pm 0.03$ . Average RI in obstructed kidneys was  $0.71 \pm 0.04$ , and in contralateral unobstructed kidneys  $0.59 \pm 0.03$ . These findings confirm rise in the intrarenal blood flow impedance in the pathologic state of renal obstruction.

Key words: renal artery-ultrasonography; ureteral obstruction

#### Introduction

Extensive research has been done in Doppler evaluation of intrarenal blood flow in transplanted kidneys. Normal values have been established, and changes of Doppler indices described in various pathologic states of transplanted kidneys.<sup>1-4</sup> These pathological changes include findings of increased resistance indices (RI) and pulsatility indices (PI) in ureteric obstruction of transplanted kidney.<sup>5</sup> Correlation between changes in the Doppler spectra and increased intrarenal impedance has been confirmed experimentally, using microsphere embolization of canine renal allografts. The correlation coefficient between blood flow estimated invasively

Corespondence to: Boris Brkljačić MD, KB Merkur, Klinčki zavod za radiologiju, Centar za ultrazvok, Zajčeva 19, 41000 Zagreb, Croatia.

and by Doppler was very good at 0.93.<sup>6</sup> There are only few recent papers considering changes in doppler spectra of intrarenal arteries in cases of obstruction of the native kidneys, and data are collected on a relatively small number of patients. It has been reported that the obstruction of the native kidney produces an increased impedance to blood flow and consequently, a rise in the Doppler-sonographic resistance indices.<sup>7,8</sup> We have assessed prospectively RI in intrarenal arteries of twenty four healthy volunteers and fifteen patients with unilateral kidney obstruction. The purpose of the study was to evaluate the role of pulse-wave and color-Doppler ultrasound in the assessment of obstructed kidneys.

#### Materials and methods

Between January 1992 and December 1992 we performed pulsed-wave and color-Doppler exa-

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mination of intrarenal arteries in 24 patients without renal impairment. Some were studied in the course of abdominal ultrasound examination performed for other reasons, whereas other were volunteers; 12 were men, and 12 women, their age ranging from 20 to 71 years with an average age of 45.6 years.

We also studied 15 patients with unilateral urinary tract obstruction, measuring RI from the obstructed and contralateral unobstructed kidneys. Seven patients were women, and eight men, with an average age of 41.2 years, ranging from 27 to 65 years. Unilateral urinary tract obstruction was caused by neoplasms in two patients (one transitional cell carcinoma of the bladder and one ovarian cancer) and by ureteral calculi in others. Ureteral calculi were mostly situated at the vesicoureteral junction, which was determined by infusion urography. Ultrasonic examination was performed in 13 patients prior to and in 2 patients secondary to intravenous urography. Ultrasonic finding of renal collecting system dilatation was shown in 14 patients, but reduction of parenchimal thickness below 11mm was not found in any of these patients. In one patient collecting system dilatation was not remarkable ultrasonically, but a stone was found in the ureter on urography.

Real time and color-Doppler examination was performed with a 3.75-MHz transducer (Radius CF machine, General Electric-CGR), and a pulsed Doppler evaluation of segmental, interlobar and arculate arteries was performed in each patient. We performed at least two measurements in consecutive waveforms in each of three intrarenal arteries, on two different sites inside the kidney, and calculated average resistance indices for each kidney from all measurements. We used the lowest wall-filter of 50 Hz and sample volume gate was 2-4 mm. RI (peak systolic frequenca shift - lowest diastolic frequency shift/peak systolic frequency shift) was calculated by the computer after hand positioning of callipers, and values were displayed on the screen.

Statistical analysis was performed by means of oneway analysis of variance (ANOV) and by desciptive statistical parameters. Statistical testing was performed using standard PC programme SPSS/PC +, and data base for patients was created in the standard programme DBASE 3 +. For graphical presentation of data we have used standard Harvard Graphics PC programme.

#### Results

The average RI in 48 kidneys of 24 examinees without renal impairment was 0.59 (1SD  $\pm$  0.03). Minimal RI value in this group of examinees was 0.53, and maximal RI value was 0.67.

The average RI in 15 unilaterally obstructed kidneys was 0.71 (1SD  $\pm$  0.04); range 0.62–0.74. In 15 contralateral unobstructed kidneys average RI was 0.59 (1SD  $\pm$  0.03); range 0.54-0.66. (Figure 1).

One-way ANOV shows a significant difference in the values of RI in the groups of obstructed kidneys vs. contralateral nonobstructed kidneys (F-ratio = 98.99; p < 0.01), and in the groups of normal kidneys vs. obstructed kidneys (F-ratio = 121.56; p < 0.01). There, is no statistical significance between RI values in the groups of normal kidneys vs. nonobstructed contralateral kidneys.

Among 15 unilaterally obstructed kidneys, in 5 kidneys (33.3 %) average intrarenal RI was <0.7. Maximal RI in the group of obstructed kidneys was 0.74.

It is important to observe that in all obstructed kidneys RI values were higher in comparison with contralateral unobstructed kidneys. The histogram showing RI values in obstructed and nonobstructed kidneys of all patients is presented in Figure 2.

However, the observed differences in values were very variable and elevation of RI in obstructed kidneys was ranging from 10.3% to 37.0% of values of nonobstructed kidneys. Figure 3 shows a B-mode image of renal pelviceal dilatation and doppler spectrum obtained in the interlobar artery of that kidney, with only slightly elevated RI in comparison with the contralateral unobstructed kidney. The spectrum from interlobar artery of the contralateral kidney is shown in Figure 4.

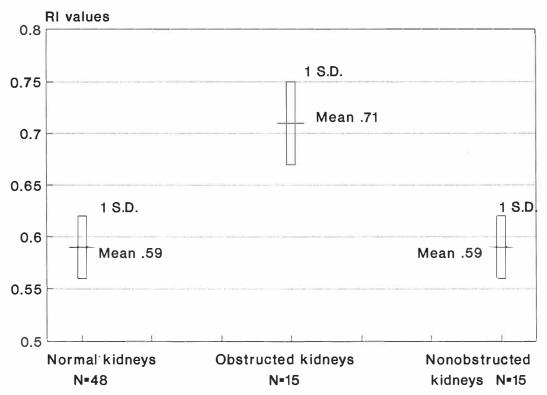


Figure 1. Display of mean RI values  $\pm$  1 S. D. in examined group of patients.

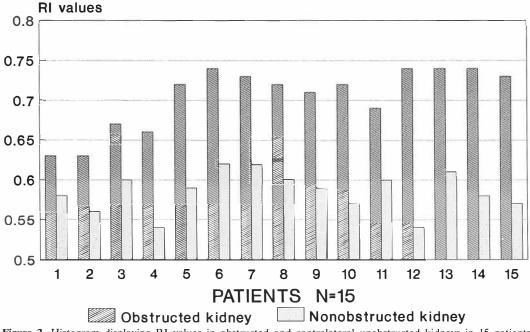
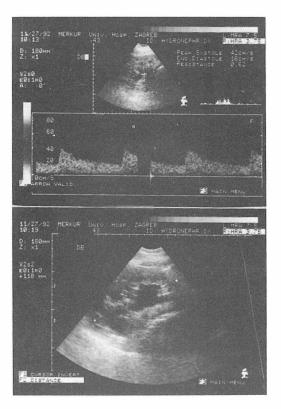


Figure 2. Histogram displaying RI values in obstructed and contralateral unobstructed kidneys in 15 patients with unilateral obstruction.



#### Discussion

The role of B-mode ultrasonic imaging in patients with acute renal colicky pain is limited to determination of pelvicocaliceal dilatation, because it is usually impossible to visualise calculi inside the ureter. Employment of Color-Doppler has enabled us to differentiate easily minor collecting system dilatations from renal vasculature, and pulse-wave Doppler studies have been performed extensively in transplanted kidney imaging. It has been reported that differentiation between ureteric obstruction and non-obstructed dilatation in transplanted kidneys was possible by pulse-wave Doppler,<sup>5</sup> which could make it possible to avoid invasive interventional studies, usually necessary in order to differentiate between these two conditions, since B-mode ultrasound is known to

**Figure 3.** B-mode ultrasonic image of mild to moderate pelviceal dilatation without reduction of renal parenchymal thickness and Doppler spectrum from interlobar artery of the same kidney with RI value of 0.62.

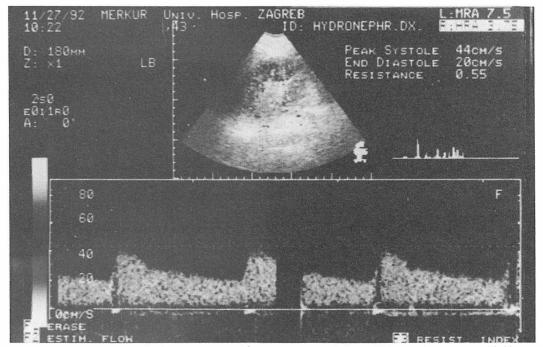


Figure 4. Doppler spectrum from interlobar artery of contralateral nonobstructed kidney with RI value of 0.55.

have false-positve results of examinations for obstruction.<sup>9,10,11</sup> However, it is necessary to rembember that the elevation of Dopler-sonographic indices is not specific for obstruction, since it is commonly found in acute rejection (especially acute vascular rejection) and sometimes in acute tubular necrosis.

There are very few studies dealing with elevation of RI in native obstructed kidneys. Platt has reported the obstruction of native kidneys as a cause of increased impedance to the blood flow, and he considers RI measurement in intrarenal arteries as useful additional evaluation tool in differentiation of the true obstruction from the nonobstructive dilatation of the renal collecting system (7). Gottlieb has reported substantial elevation of resistance indices in four obstructed kidneys, in comparison with contralateral unobstructed kidneys and normal controls.<sup>8</sup> In all four patients Doppler was preceded by intravenous urography and authors speculated about the possibility of osmotic diuresis following intravenous contrast application affecting RI by alternating blood flow to the kidney. Conversely, we performed ultrasonic examination prior to urography in most of our patients with ureteric obstruction, and B-mode ultrasonic and Doppler findings have initiated further imaging. The fact that we have found substantially lower average resistance indices in obstructed kidneys in comparison with previously reported studies indicated that there might be a certain role in the intravenous contrast application affecting the blood flow impedance. In addition, our patients had no reduction of renal parenchymal thickness, implying lack of major functional changes caused by obstruction, which could also perhaps explain lower values of RI found in our study. We have also examined arcuate and segmental intrarenal arteries blood flow spectral waveforms, in addition to arcuate or interlobar arteries studied solely in pervious studies. Therefore, we believe that we have obtained more precise assessment of intrarenal blood flow impedance in normal and obstructed native kidneys.

Real-time, ultrasound determined mild, moderate or severe pelveocalyceal dilatation in 14 of 15 kidneys with acute obstruction. In one patient with renal colicky pain the ultrasonic finding of kidney collecting system dilatation was not remarkable, although a stone was visualised in the ureter on infusion urography. In this kidney RI was also slightly elevated, indicating that this elevation might precede collecting system dilatation. More patients should be studied to assess whether it is the real cause of events in acute obstruction.

The mechanism of elevation of RI and PI in obstruction is not known, but it might be the result of an inreased interstitial pressure in the kidney, caused by urinary tract obstruction. Additionally, prolonged ureteral occlusion produces an increase in renal weight from edema, as shown in experimental studies on dogs.<sup>12, 13</sup>

The possible limitations of our study include relatively small number of patients, too small to define a threshold RI value for renal obstruction. Unlike previous studies, we have shown that values of RI < 0.70 do not exclude renal obstruction, since a third of our patients had RI below 0.70. We believe that the comparison of RI in the obstructed and contralateral non-obstructed kidneys is much more valuable for diagnosis of urinary tract obstruction, since we have found in all patients that values of RI in obstructed kidneys were higher for more than 10 % in comparison with nonobstructed kidneys.

It should be kept in mind that pathologic processes other than obstruction may cause an elevation of RI, and that Doppler findings have to be assessed together with other imaging modalities and clinical data. Also, patients with partial obstruction may show values of Doppler indices that overlap with values in kidneys of healthy patients. The intrarenal arteries of normal native kidneys have a characteristic Doppler spectral waveform, with continuous antegrade, relatively high diastolic flow, spectral broadening and clearly definable normal range of resistive and pulsatility indices. Significant elevation of RI in acutely obstructed native kidneys in comparison with nonobstructed contralateral and normal native kidneys, although

representing an unspecific finding, indicates that it is useful to introduce Doppler examinations of intrarenal arteries in the course of diagnostic work-up in cases of renal colicky pain and in cases of ultrasonically visible or suspected pelvic or pelveocalyceal dilatation, even prior to proceeding to intravenous urography. Since normal RI strongly speaks against obstruction, color-Doppler is very useful in cases of suspected pelveocalyceal dilatation with normal RI for imaging renal sinus vasculature, that might mimic pelviectasis.

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# Contribution to the treatment of lymphoceles after renal transplantation

### Željko Fučkar,<sup>1</sup> Anton Maričić,<sup>1</sup> Vladimir Mozetič,<sup>2</sup> Damir Dimec<sup>1</sup>, Damir Miletić<sup>3</sup>

<sup>1</sup> KBC Rijeka, Clinic for Surgery, Department of Urology – Rijeka, Croatia
 <sup>2</sup> Faculty of Medicine, KBC Rijeka, Ultrasound Unit – Rijeka, Croatia
 <sup>3</sup> KBC Rijeka, Department of Radiology – Rijeka, Croatia

Lymphocele is one of the surgical complications following renal transplantation, which requires immediate diagnosis and treatment. In the period between 1972 520 renal transplantations were done, at the Clinic of Surgery KBC Rijeka (loc. Sušak). Lyphoceles were diagnosed in 17 (3.2%) patients. Percutaneous drainage with instillation of povidone-iodine in 10 (58%) patients, or tetracycline in 1 (6%) patients – as sclerozating devices – and percutaneous aspiration in 3 (18%) patients were used as therapeutic procedures. All procedures have been conducted under ultrasound guidance, which was also used in the follow up. Surgical intervention was necessary in 3 (18%) patients. The authors – presenting theirs results in correlation with those from literature – emphasized significance of ultrasound in the diagnosis, treatment and follow up of lymphoceles after renal transplantation.

Key words: kidney transplantation-adverse effects; lymphocele-therapy

#### Introduction

The retroperitoneal area, surrounded with iliac blood vessels, is filled with lymphatic vessels. Lymphocele is a known surgical complication which occurs most frequently after pelvic or retroperitoneal lymphadenectomy and renal transplantation.

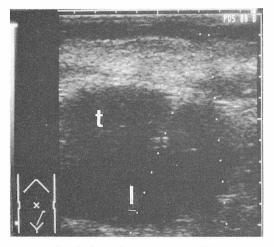
Surgery in this area demands precise tying of lymphatic vessels to prevent lymph secretion into the operative field. A comparison of creatinine levels in serum, urine and drainage fluid

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confirmed the presence of lymphatic collection. Lymphoceles, which rise in nearly 3% of patients with transplanted kidney, are commonly diagnosed within few weeks after transplantation.<sup>1</sup> Lymphoceles could produce infection or compression on pyelocaliceal system (Firuge 1) with progressive regression of transplant function.<sup>2</sup>

Precise diagnosis is provided by ultrasound examination. On sonolaminograms lymphocele is shown as an anechoic or hypoechoic focal lesion with occasional septa and internal echoes<sup>3</sup> (Figure 2). Ultrasonically guided percutaneous aspiration punction drainage with instillation of povidone-iodine or tetracycline, omentoplastic or marsupialization are methods used in the treatment of lymphoceles.<sup>4</sup>

Correspondence to: Željko Fučkar MD, KBC Rijeka, Clinic for Surgery, Department of Urology – Rijeka, Croatia.



**Figure 1.** Semioblique linear scan of the kidney transplant (t) with a voluminous lymphocele (l).

#### Methods and results

From 1972. to 1992., 520 kidney transplantation (311 from living donor, 219 cadeveric) had been done at the Clinic for Surgery of KBC Rijeka (loc. Sušak). Lymphoceles were diagnosed in 17 (3.2%) patients, nine (56.7%) of these in cadaveric transplants and eight



**Figure 2.** Oblique linear scan of the kidney transplant (t) with a dilatated ureter (u) and pyelocaliceal system compressed with lymphocele near lower pole (l).

(43.3%) in living donor transplants. The number of diagnosed lymphoceles corresponded to those in the recent literature (Table 1).

Ultrasound as a diagnostic method was introduced in our Clinic in 1975. Several types of ultrasound equipment were used: "Fischer-Emsonic", "Bruel and Kjaer-Model 1840", "Aloka SSD 220 LS" and "Hitachi EUB 515", with sector and linear probe of 3.5 and 5 MHz. The size of lymphoceles ranged from  $3 \times 2$  cm of those with different localization, to those which involved whole kidney. Simple lymphoceles were prevalent; only in 3 (17%) patients were they septate (Table 2).

Percutaneous drainage with povidone-iodine or tetracycline sclerosation and percutaneous aspiration – both under ultrasound guidance – or surgery were used as therapeutic methods (Table 3). Percutaneous drainage with sclerosation was performed in the following way: the patient lied in the supine position. Sterilization and confining of the operative field were done with standard solution and sterile compresses.

 Table 1. Comparison of posttransplant lymphoceles diagnosed by different authors.

Authors	# trans- plantation	Lymphoceles
Moukarzel and all.	1000	14 (1.4%)
Meyers	132	4 (3.03%)
Calahorra and all.	107	8 (7.4%)
KBC Rijeka/lok. Sušak	520	17 (3.2%)

 Table 2. Localization of lymphoceles in correlation with transplant.

Upper pole	4	(23%)
Lower pole	7	(41 %)
Anterior side	3	(17%)
Arround transplant	3	(17%)
Total	17 (1	100 %)

 
 Table 3. Methods used in the treatment of lymphoceles.

10 (58%)
<b>、</b>
1 (6%)
3 (18%)
3 (18%)

The best position was fixed with a sterilized ultrasound probe. A skin incision (2–3 mm) was done under a local anesthesia. The lymphocele was set in the position which corresponded to the puncture-line of the probe (Figure 3). An



Figure 3. Linear scan of lower part of the kidney transplant (t) with lymphocele (l) prepared for puncture.



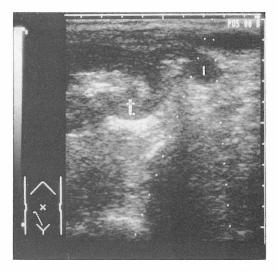
**Figure 4.** Linear scan of the same lymphocele during instillation of povidone-iodine. Light hyperechoic area (arrows) corresponds to the needle top surrounded with povidone-iodide.

aspiration was done through a 22 gauge needle, which followed the puncture line; the procedure started with aspiration, and after that, through the same needle, povidone-iodine or tetracycline was instilled (Figure 4). The initial result of sclerosation was seen half an hour after the instillation (Figure 5). The complete sclerosation was folloved by a regular ultrasound examination.

Complications after treatment – febrility, epididymitis or recurrence – were found in 4 (21%) patients (Table 4).

#### Discussion

Ultrasound is the most common diagnostic method used for diagnosing lymphoceles after a renal transplantation. Koizumi et al.<sup>5</sup> described a scintigraphic finding of lymphocele after Tc99



**Figure 5.** Linear scan of the same lymphocele (I) in the lower part of transplant (t), half an hour after instillation of povidone-iodine, showing partial sclerozation.

 Table 4. Complications after the treatment of lymphoceles.

1 (5%)
1 (5%)
2 (11%)
4 (21%)

application in patients with postoperative complications after a renal transplantation. Perirenal photon insufficiation was shown. Lymphoceles are usually discovered within 6 weeks after the transplantation. Thompson and Neale<sup>6</sup> described a patient with posttransplantation lymphocele discovered 8 years after transplantation. Schuraritzky et al.<sup>7</sup> showed their own experience with 13 aspiration punctions of lymphoceles with 9 (63%) recurrences. Percutaneous drainage was done in 29 patients. In 16 (55%) no further therapy was necessary. In 8 patients recurrence was treated by marsupialization, whereas the percutaneous drainage was repeated in 5 patients. Fibrous glue (5 ml) was installed in 8 cases. Complications, e.g. infection, were found in 5 patients. Moukarzel et al.<sup>8</sup> suggested marsupialization and omentoplastica as the method of choice in voluminous lymphoceles. Calahora et al.9 considered percutaneous interventions in peritransplant collections as a definitive treatment methods. Gilliland et al.<sup>10</sup> reported that percutaneous treatm ent of 9 lymphoceles with povidone-iodine instillation was 89% successful.

At the Clinic for Surgery, KBC Rijeka (loc. Sušak), 520 kidney transplantations were done in a twenty-year period. Lymphoceles were diagnosed in 17 (3.2%) patients. Fourteen ultrasonically guided interventions (11 percutaneous drainages with instillation and 3 percutaneous aspirations) and three surgical interventions were performed. Morbidity and mortality in patient with a kidney transplant were decreased after the use of percutaneous treatment. Percutaneous aspiration and drainage with instillation of povidone-iodine or tetracycline proved to be successful, and the authors recommend it as a method of choice in the early treatment of lymphoceles.

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## Renal blood flow measurement from first pass time-activity curves in patients undergoing routine bone scintigraphy

Dražen Huić, Darko Grošev, Damir Dodig, Mirjana Poropat, Darko Ivančević

Clinical Department of Nuclear Medicine and Radiation Protection University Hospital Rebro Zagreb, Croatia

We measured renal blood flow (RBF) as a fraction of cardiac output (CO) by using Tc 99-m methylene diphosphonate (Tc-99m MDP) in 41 patients undergoing routine bone scintigraphy for a variety of indications. All patients were without evidence of renal disease. Twenty-nine left kidneys were normal in size and shape with a mean RBF/CO value  $10.6\% \pm 2.2$ . Twenty-seven normal right kidneys had a mean RBF/CO value  $9.8\% \pm 1.9$ . Twenty-one patients were with both kidneys of normal appearance, with a mean RBF/CO value  $20.9\% \pm 3.4$  for both respectively. The arterial regions of interest (ROIs) were generated from the right lung, left ventricle (LV) and upper abdominal aorta. A mean RBF/CO value calculated from right lung ROI was consistently less than that obtained from LV, with a mean ratio of  $0.86 \pm 0.11$ . A mean ratio between RBF/CO values from aorta and LV was  $1.05 \pm 0.13$ . Our results closely agree with those of other authors, so we have concluded that this method could be very useful in clinical practice, whenever the estimation of renal blood flow is needed.

Key words: bone diseases-radionuclide imaging; renal circulation; blood flow velocity

#### Introduction

It is well known that renal blood flow (RBF), differential renal function and even renal anatomy may be evaluated with Tc-99m methylene diphosponate (Tc-99m MDP) in patients referred for routine bone scintigraphy.<sup>1, 2</sup> In such patients RBF and renal function are often impaired.<sup>2</sup>

A. M. Peters and colleagues described a method for measuring organ blood flow as a

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percentage of cardiac output (CO) from the first pass time/activity curves obtained from regions of interest (ROIs) over the organ, and from arterial ROIs. The method determines the count rate that would be recorded over the organ if the tracer behaved like radiolabelled microspheres, and was totally trapped in the organ vascular bed on the first pass.<sup>3-5</sup> This technique has been used in several investigations such as renal transplant rejection,<sup>6</sup> renal artery stenosis,<sup>7</sup> and cyclosporin nephrotoxicity.8

The aim of this paper is to evaluate this method in patients undergoing routine bone scintigraphy, and to compare RBF/CO values based on the right lung ROI, left ventricle ROI

Correspondence to: Dr. Dražen Huić, Zavod za nuklearnu medicinu Medicinskog fakulteta, Klinička bolnica Rebro, Kišpatićeva 12, 41000 Zagreb, Croatia.

and aorta ROI. We also compared the perfusion renal images and RBF/CO values with the static renal images obtained during bone scintigraphy.

#### Patients and methods

We examined 41 patients (21 females, 20 males; mean age 55) referred to our department for routine bone scintigraphy. Thirty of these were referred for suspected bone metastases, five for suspected osteomyelitis, three with arthritis and three for possible sacroiliitis. All patients were without evidence of renal disease. A majority of kidneys (N = 56) appeared normal in size and shape on summed perfusion scintigram. The other kidneys were smaller and poorly visible (N = 26).

The dose of Tc-99m methylene diphosponate (Tc-99m MDP, activity of 550 MBq) was injected rapidly as a compact bolus. After injection, data were acquired at 1s per frame for 60s. Patients were placed in supine position and the gamma camera was positioned posteriorly over the upper abdomen and lower chest. Data were stored on digital computer for later analysis. Pre- and post-dose syringe counts were measured on collimated gamma camera face as a 10 second static images for measuring net injected dose. Growing syringe activities in a range from 37 MBq to 800 MBq were measured for a dead-time correction. A curve of the measured versus true count rate which is typical for paralizable counting systems was obtained. By iterative method we estimated true count rates based upon measured and a dead time parameter, determined by nonlinear regression (Figure 1).

Lateral views were made for depth correction (the distance between the posterior abdominal wall and the center of the kidney was marked) during bone scintigraphy, about 3 hours after injection. The obtained distance (x) was later used as depth correction factor.

Data analysis was performed by using curves obtained over the right lung, left ventricle, abdominal aorta and kidneys (Figure 2). RBF as a fraction of CO was finally calculated form the folloving formula:<sup>3, 4</sup>

$$\frac{RBF}{CO} = \frac{gk}{ga} \frac{A}{D} DCF \times 100$$

Where RBF/CO = RBF as a percentage of CO; gk = maximum upslope of renal curve; ga = maximum upslope of integrated aortic curve; A = plateau of integrated aortic curve (cts/sec); D = net injected dose; DCF = depth correction factor ( $e^{\mu x}$ ),  $\mu$  = Tc- soft tissue linear attenuation coefficient (0.153 cm<sup>-1</sup>).

A final RBF/CO value was expressed as an average value of there estimates from three arterial ROIs. RBF/CO values obtained on the lung ROI and aorta ROI curves from all 82 kidneys, were then expressed in the corresponding ratio for the LV curves. Values are expressed as a mean value  $\pm$  standard deviation. Statistical analysis was performed by using t-test.

#### Results

The total of 82 kidneys were analysed and RBF/CO values calculated. Twenty-seven right kidneys and 29 left kidneys were normal in size and shape with the mean values of RBF/CO  $9.8\% \pm 1.9$  and  $10.6\% \pm 2.2$ . Poorly appeared and small kidneys (14 right and 12 left) had average values of RBF/CO  $5.2\% \pm 1.5$  and  $5.6\% \pm 1.3$  respectively. The differences between right and left kidneys were not significant (p>0.05). Twenty one subjects were without evidence of any renal disease, with both normal kidneys. A mean RBF/CO value for both kidneys was  $20.9\% \pm 3.4$ .

RBF obtained on the right lung ROI was less than that obtained on the LV ROIs, with a mean ratio of  $0.86 \pm 0.11$ , thus being significantly different (p<0.001). RBF based on the abdominal aorta was greater than that obtained on the LV ROI, with the mean ratio of 1.05  $\pm$  0.13, which is also significantly different (p < 0.01). The delayed renal images corresponded well with the RBF/CO values and early renal images in 75 (91%) kidneys. Seven kidneys

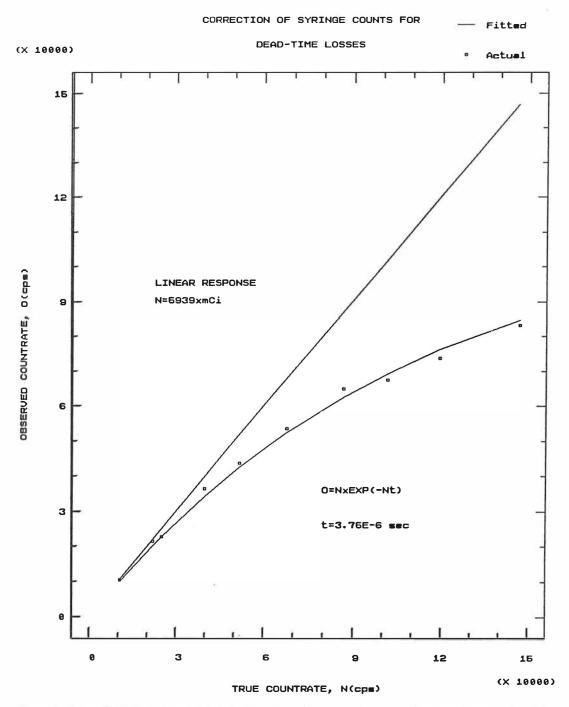


Figure 1. Curve fitted through experimental data-points of true vs. observed syringe count rates along with linear response. The obtained curve served for estimation of the true count rate from the observed by iterative method.

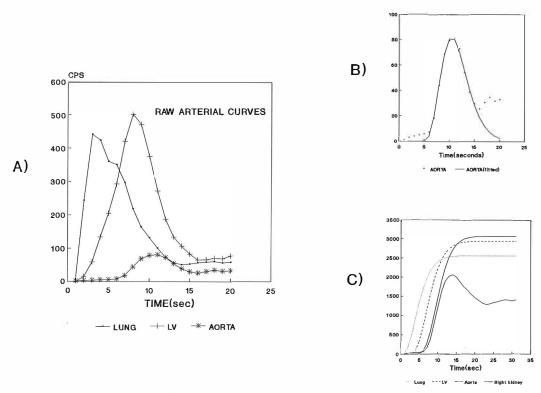


Figure 2. A) Raw arterial curves drawn from corresponding ROIs. B) Smoothed LV curve along with fitted gamma-variate curve. C) Integrated fitted arterial curves multiplied by corresponding  $g_k/g_a$  ratio to obtain parallelism with the upslope of kidney curve.

(9%) appeared normal during bone scintigraphy, but their RBF/CO values were low.

#### Discussion

Our results with 99m Tc-MDP confirmed the postulate that noninvasive measurement of organ blood flow which is based on the principle of fractionation of cardiac output is applicable with any recirculating gamma emitting tracer.<sup>4</sup>

In our investigation, the mean RBF/CO value from the normal left kidney was greater than the value obtained from the normal right kidney, but not significantly (p>0.05). A. M. Peters et al. obtained RBF/CO value for the normal left kidney 10.4%  $\pm$  1.2 and 11.4  $\pm$ 1.3 by using Tc-99m DTPA in two separate papers. RBF/CO value for the normal right kidney was 9.0%  $\pm$  1.1 and 9.9%  $\pm$  1.1. The difference between left and right kidneys was significant, probably resulting from splenic overlap.<sup>4, 7</sup> The splenic inflow appears early and sometimes it is very difficult to distinguish the left kidney margin from the splenic margin. In the study performed with Tc-99m Mag3 the RBF/CO the values were similar (right kidney  $8.5\% \pm 1.1$ ; left kidney  $9.7\% \pm 0.8$ ; both normal kidneys  $18.3\% \pm 1.5$ ).<sup>9</sup>

We obtained a similar difference between the RBF values based on lung, LV, and aorta ROIs like Bell and Peters, but our lung/ LV ratio was smaller. They report lung/LV ratio  $0.94 \pm 0.14$ ; (p < 0.001), and aorta/LV ratio  $1.05 \pm 0.18$ ; (p < 0.01).<sup>8</sup> We did not correct the LV curve for the lung activity because that procedure decreases statistical accuracy and it is probably the reason for our lower value.<sup>10</sup>

It is important to say that the lung time-acti-

vity curves were very easy to fit and gave the cleanest curves (relatively later appearance of re-circulation). The LV curve is contaminated by activity in the left base of the lung while the aortic curve is often contaminated by the activity from the inferior vena cava. So in the case that the LV and aortic curves are too noisy, RBF value from lung curve should be multiplied by factor 1.16 (1/0.86) and 1.22 (1.05/0.86) to get a correct LV and aortic RBF/CO value, respectively.

It is really surprising that even 26 (32%) kidneys were poorly displayed, with low RBF/CO values in patients without evidence of renal disease. The reasonable explanations could be patients' age, primary disease and side effects of therapy.

The simplicity of the procedure and results in physiological units render this method useful in clinical practice, and it could be useful in patients undergoing routine bone scintigraphy if they are under suspicion of poor renal blood flow.

It is possible to get indirect information about RBF from static renal images obtained during bone scintigraphy. In such evaluation one should be very careful with respect fo the fact that seven normal appearing kidneys had low RBF/ CO values in our investigation.

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# To the problem of second primary tumor in long-term survivors of small-cell lung cancer

# **Miha Debevec**

Institute of Oncology, Ljubljana, Slovenia

Two cases of second primary tumor (SPT) of the lung after multimodality treatment of small-cell lung cancer (SCLC) are presented. In both of them non small-cell lung cancer (NSCLC) was stated. The frequency of lung SPT is discussed.

Key words: lung neoplasms; carcinoma, non-small cell lung; neoplasms, second primary

# Introduction

Warren and Gates<sup>1</sup> stated that a cancer patient may be "cancer prone" and tends to develop new primary cancer more frequently than do patients their first cancer. On the other side, the cases of multiple primary carcinomas in the same region and elsewhere in the body are becoming increasingly common.

Current multimodality approaches to the management of patients with small-cell lung cancer (SCLC) improved their survival rates. With an improved potential for care and accrual of long-term survivors of SCLC, the adverse effect of chemo- and radiotherapy, and a higher incidence of second primary tumors (SCT) have become apparent.

In the article two cases of SCLC patients are presented; in one of them SPT was metachronous non small-cell lung cancer (NSCLC), and in another patient it was probably synchronous double lung cancer. The problem of frequency of SPT of the lung is discussed.

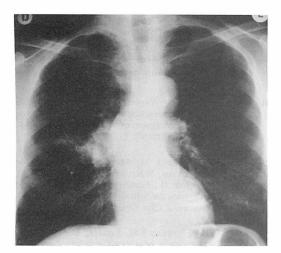
# Case No. 1

A 68-year old male patient (Pat. rec. # 6718/82) was operated on for a 2-cm peripheral SCLC of the upper left lobe in September 1982. The stage of tumor was  $pT_1N_0M_0$ . Postoperatively, seven applications of chemotherapy (cyclophosphamide, vinblastine, methotrexate, 5-fluorouracil) were performed. In September 1988, tumorous infiltration of the left hilus was evident on chest x-ray. In December 1988, bronchoscopy was performed: there were signs of lower left bronchial tumor and large-cell carcinoma confirmed. The patient died in December 1990 due to progression of lung cancer and liver metastases, i. e. 99 months after surgery for small-cell carcinoma, and 27 months after the diagnosis of large-cell carcinoma.

# Case No. 2

In May 1989, a 65-year old male patient (Pat. rec. # 2195/89) presented with small cell carcinoma of the lower right robe (Figure 1). Clinical stage of the tumor was  $cT_2N_2M_0$  (limited disea-

Correspondence to: Prof. Miha Debevec, MD, Ph. D. Institute of Oncology, Zaloška 2, 61105 Ljubljana, Slovenia.



# Figure 1.

se). After six applications of chemotherapy (cyclophosphamide, doxorubicin, vincristine) radiation therapy with TD 45 Gy (2.5 Gy daily, split course regimen) was performed. On bronchoscopy in February 1990 there were no more signs of bronchial tumor, but brushing of the right lower lobe showed cells of large cell carcinoma, whereas chest x-ray was unsuspicious (Figure 2). The patient was observed, and in January 1993 bronchoscopy was performed because of a progressing tumor of the left hilus, which revealed large-cell carcinoma in the apical segment of the lower left bronchus. In the right bronchial tree there were no signs of tumor (Figure 3). So, the cytological diagnosis of NSCLC was established 9 months after diagnosis of SCLC.

### Discussion

The lung is one of the organs in which multiple primary cancers occur very often. Moreover, the lung is the most common site in patients with double cancer.<sup>2</sup>

Improved survival of SCLC patients after therapy results in an increased number of SPT cases. Criteria for the differentation of new lung lesion as SPT are: 1) different histological type, 2) different lobe, and 3) time interval of at least two<sup>3</sup> or three<sup>4</sup> years.

Sagman et al.<sup>5</sup> found 30 SPT in 800 SCLC patients – in 6 of them the SPT was NSCLC, and suggested that increased predisposition to SPT may be attributed to secondary effects of multimodality treatment and biological considerations although 2/6 SPT were classified as synchronous, i. e. SPT developed within 1 year.

Heyne et al.<sup>6</sup> estimated 14 SPT in 446 patients with SCLC, 6 of them NSCLC, and considered long-term survivors of SCLC as excellent candidates for chemoprevention trials.

Osterlind et al.<sup>7</sup> reported 13 SPT among 72 SCLC long-term survivors; 5/13 were NSCLC.

Souhami and Law<sup>8</sup> found only 8 SPT in 217 two-year survivors with SCLC; 1/8 was NSCLC.

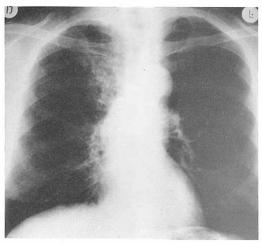






Figure 3.

Case No. 1 is undoubtedly a secondary primary NSCLC after successful treatment for SCLC: different histology, different lobe, and more than 3-year interval between the appearance of both tumors.

Case No. 2: it would have corresponded to these criteria too, had there not been bronchoscopy performed 9 months after the diagnosis of SCLC. Although NSCLC cells were taken by brushing biopsy from the right site, probably they arise from the tumor of the left lower lobe verified 3 years later. Therefore, this case is most probably synchronous double primary lung tumor. Regarding the doubling time of lung cancer, Marmorschtein et al.9 consider all lung tumors found within 3 years as synchronous. So, we could not regard Case No. 2 as SPT due to chemo- and radiotherapy for SCLC. Accordingly, the relative risk of development of NSCLC as SPT, calculated in patients before three years from diagnosis of SCLC,<sup>5,6,7</sup> seems to be exaggerated.

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# The rate of natural killer cells and their cytotoxic activity in patients with advanced pharyngeal and laryngeal cancer

Lojze Šmid, M Žargi, B Rok, A Župevc, V Kotnik, A Ihan, M Rode

University Department of Otorhinolaryngology and Cervicofacial Surgery, Clinical Center Ljubljana, Slovenia

The activity of natural killer (NK) cells was assessed In 46 patients with previously untreated advanced squamous cell carcinoma of the head and neck region. The mean NK cell activity of these patients was lower than that observed in a group of 32 age-matched controls (62.5 vs 90), however, the difference was not statistically significant. Patients with regional metastases that grew through the lymph node capsule and those with primary tumor directly invading the surrounding tissue had significantly lower values of NK cell activity than patients with locoregionally controlled tumors (p = 0.02).

Key words: pharyngeal neoplasms; laryngeal neoplasms; killer cells, natural

# Introduction

The role of natural killer (NK) cells in patients with malignomas of the head and neck has not been fully explained yet. Many facts support their possible influence in the destruction of circulating tumor cells,<sup>1</sup> and some authors believe that a decreased cytotoxic activity (CA) of these cells attributes to the appearance of distant metastases.<sup>2–5</sup> The latter observation seems to be of particular importance and interest in the case of patients with head and neck tumors, as such indicators of the probability of distant metastatic spread would be very helpful for correct treatment selection.

Correspondence to: L. Šmid, MD, University Department of Otorhinolaryngology and Cervicofacial Surgery, Zaloška 2, 61105 Ljubljana, Slovenia

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In our prospective study we were determining the number of NK cells and their CA in the peripheral blood of patients with advanced laryngeal and pharyngeal cancer, in order to asses their possible relevance for prognosing the course of disease.

#### Methods

The study was carried out in 46 patients, 40–81 years of age, with previously untreated and histologically confirmed advanced carcinoma of the pharynx and larynx. The disease was classified as stage 3 or 4 in all patients.<sup>6</sup> In 23 of them the site of origin was the oropharynx, in 15 hypopharynx and in 8 larynx. The prevailing histologic type was poorly differentiated or non-keratinizing planocellular carcinoma (37 patients), whereas well differentiated keratinizing planocellular carcinoma yeas established in 9

cases. Twenty-two patients were treated by radiotherapy, 20 were operated on – of these 18 also received postoperative irradiation, and 4 patients were treated by a combined radioand chemotherapy.

The control group consisted of 32 patients admitted to the University Department of Otorhinolaryngology and Cervicofacial Surgery because of some other, non-malignant diseases; the controls were matched to the studied cancer patients by age and sex.

CA of NK cells was determined by means of K 562 tumor cell killing test. These cells were mixed with lymphocytes isolated from the peripheral blood of patients with laryngeal and pharyngeal cancer. After 4-hour incubation, the rate of killed target cells was evaluated, and calculated in lithic units, where their higher value was associated with a higher K 562 tumor cell killing potential of NK cells.

# **Results and discussion**

In patients with advanced cancer NK activity is usually depressed.<sup>7-11</sup> Also in our patients, the average CA of NK cells was lower than that observed in the control group (62.5 vs 90), though the difference between both groups was not statistically significant. The average rate of NK cells in patients with laryngeal and pharyngeal cancer was 16.1%, being lower from that in the control group, though the difference between both groups was not statistically significant.

Comparison of the average rates of NK cell counts and their cytotoxic activity by tumor site and histologic type did not show statistically significant differences, and neither confirmed a correlation between the average rate of these cells and their CA. Similarly, data from singlecell cytotoxicity assays suggest that the defect rests in the activity and not in the number of NK cells.<sup>12</sup>

Since our investigation was aimed to asses a possible prognostic relevance of NK cells, and since in patients with laryngeal and pharyngeal cancer the best indicator of the probability of distant dissemination is known to be local and regional tumor spread,<sup>13-15</sup> our analysis of the results was centred particularly on these issues. The available literary data on the CA of NK cells in patients with head and neck carcinomas are relatively scarce. There are, however, even less reports on the role and significance of CA of these cells for the appearance of local metastases. Cortesina et al.<sup>16</sup> report a decreased CA of NK cells in advanced head and neck cancers. Pross and Baines<sup>7</sup> established a decreased CA in patients with metastases in comparison with cases without regional tumor dissemination. Schantz and coworkers,<sup>17</sup> however, found an increased CA of NK cells in patients with local or regional tumor invasion of the surrounding tissue.

In our study, the average CA of NK cells in patients with regional metastases in N3 and N2 was found to be significantly lower than that in the control group (p = 0.04 and 0.05 respective-ly), whereas in patients with N0 and N1 no statistically significant difference could be established (Figure 1). The extent of local dissemination (control group – N0-N1-N2-N3 was in correlation with the values of average CA in individual groups: thus, a 5% risk was associated with negative correlation (KK = -0.274).

The comparison of NK cell rates and their CA in the group of patients with local or regional spread, and those without evidence of dissemination revealed interesting differences. In the cases when tumor did not show evidence of local or regional invasion into the surrounding tissues the rate of NK cells was on average lower than that in the group with local infiltration (13.5 vs 18.2), though the difference was not statistically significant (p = 0.08). An average CA of NK cells in the group of patients with local tumor invasion (39) was significantly lower than the relevant values in the control group (90) (p = 0.01), and borderline significantly lower than in patients without local infiltration (73) (p = 0.07) (Figure 2). Also, an average CA in the group of patients with regional invasion (44) was significantly lower than that in the control group (90) (p = 0.02) and borderline significantly lower than in the group

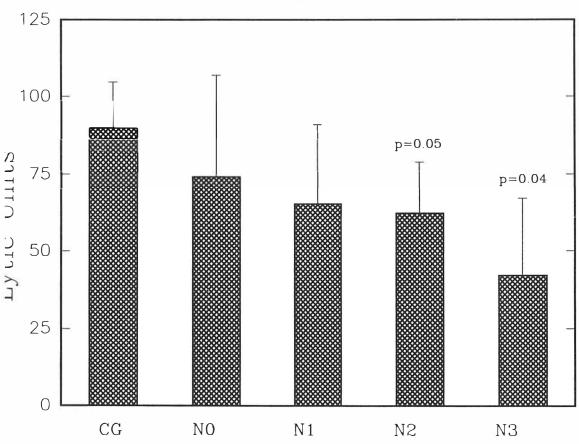


Figure 1. Mean CA of NK cells according to N stage (CG = control group).

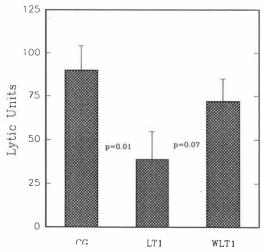


Figure 2. Mean CA of NK cells according to local tumor infiltration into surrounding tissue (CG = control group; LTI = local tumor infiltration; WLTI = without local tumor infiltration).

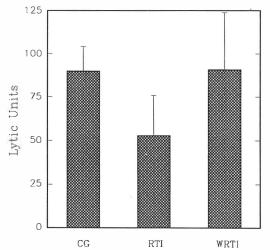


Figure 3. Mean CA of NK cells according to regional tumor infiltration into surrounding tissue (CG = control group; RTI = regional tumor infiltration; WRTI = without regional tumor infiltration).

CG LRTI WLRTI **Figure 4.** Mean CA of NK cells according to local and regional tumor infiltration into surrounding tissue (CG = control group; LRTI = local and/or regional tumor infiltration into surrounding tissue; WLRTI =  $\pm$ without local and/or regional tumor infiltration into surrounding tissue).

without regional invasion (75) (p = 0.07) (Figure 3). The difference is apparent also in the group of operated patients in whom the removed lymph nodes were histologically examined.

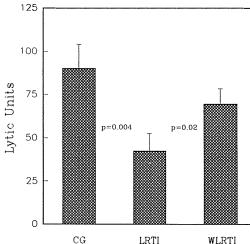
When the average CA in the group without locoregional invasion into the surrounding tissues was compared with that found in the group with locally and regionally infiltrating tumor the difference was statistically significant (p = 0.02) (Figure 4). These findings can be presented from yet another aspect: in only one of 18 patients without evidence of locoregional invasion CA was lower than 30 lithic units (LU) (5.5%). On the other hand, in the group of 28 patients with tumor invasion into the surrounding tissues CA was below 30 LE in as many as 17 patients (61%). Therefore CA lower than 30 LE could be considered as unfavourable prognostic sign.

# Conclusion

The findings of our investigation indirectly support the hypothesis that in patients with laryngeal and pharyngeal cancer the course of disease in reflected in the CA level of NK cells. Nevertheless, it should be kept in mind that our results are only preliminary, and therefore their final evaluation would require further follow up of the patients. Only in this way the hypothetical correlation between the CA of NK cells and prognosis of the disease could be confirmed.

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# Effects of irradiation and THP-Adriamycin on the proteinase activity profiles in cultured V79 cells

Danilo Petrović,<sup>1</sup> Ana Ferle-Vidović,<sup>1</sup> Janez Škrk,<sup>2</sup> Alojz Suhar,<sup>3</sup> Vito Turk<sup>3</sup>

<sup>1</sup>Ruđer Bošković Institute, Zagreb, Croatia <sup>2</sup>Institute of Oncology, Ljubljana, Slovenia <sup>3</sup>Institute Jožef Stefan, Ljubljana, Slovenia

In the present work the changes of the activities of three types of proteinases (aspartic, cystein and neutral) in proliferative Chinese hamster lung fibroblasts (V79), treated by gamma irradiation or by the cytostatic agent 4-0-tetrahydropyranil (THP) Adriamycin, were followed. Our results show, that the activities of different enzymes tested, were changed by each of the two treatments in a different way.

Key words: fibroblasts; radiation effects; dexorubicin; peptide peptidohydrolases

# Introduction

Proteolytic enzymes are essential in the cell metabolism and physiology, but they are also of crucial importance in processes involved in cellular proliferation kinetics and cell death.<sup>1,2</sup> They are an important part of gene regulation processes.<sup>3</sup> Their activity therefore, if measured when cells are in various physiological states or if they are exposed to damaging agents, may provide certain evidence about some molecular events occurring in the cells under particular circumstances.

In our previous papers we presented results indicating a correlation between the activity of intracellular proteinases and irradiation<sup>4</sup> and

Corespondence to: dr. Danilo Petrović, Ruđer Bošković Institute, Bijenička 54, Zagreb, Croatia.

UDC: 612.75.014.469.015.12

about proteinases influencing the repair of potentially lethal damage.<sup>5,6</sup>

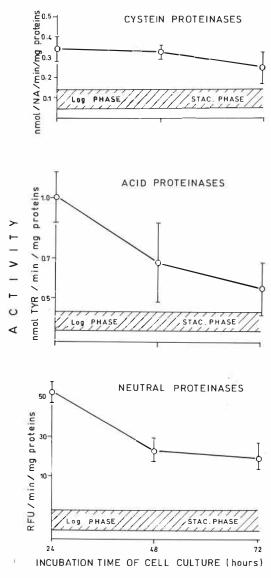
In this work we present some changes of the activities of three types of proteinases (aspartic, cystein and neutral) in proliferating Chinese hamster lung fibroblasts (V79), treated by gamma irradiation or by the cytostatic agent 4-0-tetrahydropyranil (THP) Adriamycin. The results show pronounced changes in the activities of neutral and cystein proteinases following irradiation, and changes in the activity of acid proteinases which are different and related to the particular agent. They also suggest their involvment in repair processes.

# Materials and methods

## Cell cultures and experimental procedure

Chinese hamster lung fibroblasts (V79), were cultured as monolayers in Eagle's minimal es-

sential medium, supplemented with 10% calf serum. Cell cultures were prepared by plating  $10^6$  cells per Petri dish of 10 cm in diameter, and after two days of exponential growth (doubling time 12 hours), before full confluency was reached, cells were either irradiated or treated by THP-Adriamycin. Following treatment, cell



**Figure 1.** Changes of the proteinase activities in a growing culture of V79 cells. Activities of the cystein, acid and neutral proteinases are determined at different phases of cell growth and expressed per mg of proteins.

cultures were kept at 37 °C and samples taken after different time intervals and stored at -20 °C until proteinase activity assay.

# Proteinase activity

The activity of acid, neutral and cystein proteinases were determined by the following procedure: washed cells were harvested by a rubber policeman, concentrated by centrifugation, lysed in distilled water and frozen at -20 °C untill assay. Lysed cells were sonicated and homogenized by Pierce homogenizer. The proteinase activities in homogenates were determined using substrates: 2% bovine hemoglobine at pH 3.5 for acid proteinases. N- $\alpha$ -benzoyl-DLarginine-1-naphthylamine (BANA) for cysteine proteinases and 1% calf thymus histones at pH 7.5 for the determination of neutral proteinase activity.<sup>7,8</sup>

# Irradiation

For iradiation, a Gammacell 220 (Atomic Energy of Canada Ltd) unit was used. The dose rate was 4.13 Gy/min. Cells were irradiated at room temperature and then transferred to 37 °C until harvesting.

# THP-Adriamycin treatment

THP-Adriamycin (4-0-tetrahydropyranil Adriamycin) was added to the growth medium to reach final concentration of 0.5  $\mu$ g per ml. Cells were incubated in the Adriamycin-containing medium at 37 °C for one hour and then incubated until harvesting.

# **Results and discussion**

In Figure 1 age-dependent changes of (a) cystein proteinases, (b) acid proteinases and (c) neutral proteinases in the growing culture are shown, and it is evident that in the phase of intensive cell growth acid and neutral proteinases decrease in their activity, while the cystein proteinases show a more steady-state pattern. When approaching the stationary phase, all

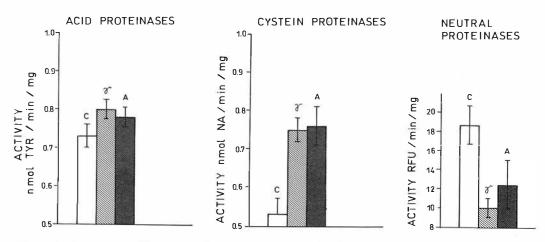


Figure 2. Proteinase activity profiles in cultures of V79 cells after gamma irradiation or treatment with THP-Adriamycin. C – Control values.  $\gamma$  – Cumulative data obtained by doses from 3-100Gy gamma rays 60 minutes following irradiation. A – Cumulative data obtained by 0.5 µg per ml THP-Adriamycin treatment for one hour. Proteinase activity was determined 60 minutes following the end of treatment.

three proteinases show a less intensive but similar decrease, and therefore this region of the culture age, with cells at the end of the exponential phase of growth was selected for treatment and proteinase activity assays. It was assumed that in this phase of cell growth the activities of all three proteinases have the most simillar patterns, thus being most convenient for comparison of the effects caused by various treatments.

Overall effects of gamma irradiation and of THP-Adriamycin on activity profiles of acid, neutral and cystein proteinases are presented in Figure 2, in order to show how treatment of each of those two agents will affect the activity of the proteinases in general. It is evident that

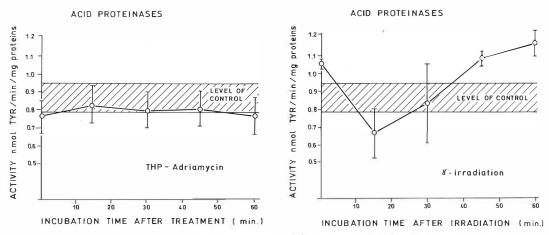


Figure 3. Time-dependent changes of acid proteinase activity cultures of V79 cells following treatment by THP-Adriamycin (a) or gamma irradiation (b). Cells were treated by THP-Adriamycin (0.5  $\mu$ g per ml) for one hour, washed, and incubated in fresh medium. Dose of gamma irradiation was 15 Gy.

if assayed 60 minutes following treatment, acid proteinases are little affected, cystein proteinases reveal increased activity while neutral proteinases are significantly depressed if compared to their controls.

In Figure 3 we analysed the effects of gamma irradiation and of THP-Adriamycin on the acid proteinase activity during the first hour following treatment. The reason for selecting this particular proteinase was the apparent absence of effects of two agents on it. The two curves show clearly, however, that the patterns of time

dependent effects are different. THP-Adriamycin did not influence the activity of the acid proteinase, irrespective of the time when the activity was measured during the one-hour period. The pattern of the effects obtain by irradiation however, shows a clear time dependence with a decrease at the 15th minute and an increase up to the 60 min. post treatment. Figure 4 shows that there is also dose-dependence of the activities of acid and cystein proteinases, if they are assayed one hour after irradiation with diferent doses of gamma rays.

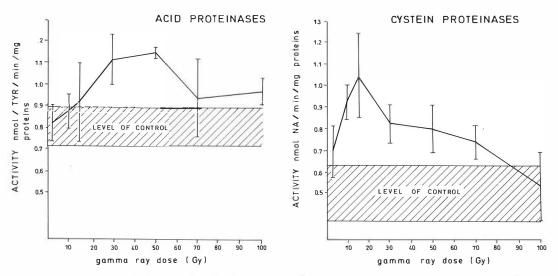


Figure 4. Dose-dependent changes of acid (a) and cystein (b) proteinase activity in cultures of V79 cells 60 minutes following gamma irradiation. Cells were irradiated, incubated for 60 minutes and then collected for proteinase activity assay.

Although they reveal different patterns, both proteinases have increased activities, significantly above the control levels, but with their maxima at different doses (50 and 15 Gy respectively), and with the tendency of decrease in the higher dose region.

The results show that the intensity of proteinase activity is dependent on the age of the cell culture, that THP-Adriamycin and gamma irradiation generally increase cystein proteinase activity and depress neutral proteinase activity, but have little influence on the acid proteinases. THP-Adriamycin has little influence on the acid proteinase activity for the first 60 minutes following treatment, but in opposite, gamma irradiation does change that activity, and finally, acid and cystein proteinase activities vary at different doses of irradiation, but in different patterns.

Genotoxic agents such as ionizing irradiation and cytostatics, commonly used in tumor therapy, damage and kill cells through different molecular mechanisms. Ionizing irradiation produces breaks in DNA molecules and this induces repair processes through activation of specific enzymes. Adriamycin, for instance as an Therefore, certain agent-related differences of the activities of intracellular proteinases were expected. According to the results presented in this work the activities of the three groups of intracellular proteinases responded in different ways to the treatments, and in brief, it can be concluded that they are an integral component of response of mammalian cells to irradiation and Adriamycin-produced damage. Which proteinases specifically are really envolved in these process, is the subject of furtner investigation.

# Acknowledgement

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Letter to the editor

# Postirradiation intraabdominal adhesions

# Marko Snoj

Department of Surgery, Institute of Oncology, Ljubljana, Slovenia

# Introduction

Intraabdominal adhesions are most frequent cause of small bowel obstruction<sup>1</sup> and female infertility.<sup>2</sup> They can be localised in any part of the bowel, but most usually they are found in the small bowel.<sup>1</sup> They occur most frequently after surgery in the abdominal cavity, seldom they are caused by peritoneal infection and even more rarely they follow irradiation of this region.<sup>3</sup>

Various experiments have been conducted for intraabdominal adhesion prevention in the past, but none gave satisfactory result.<sup>4</sup> Recently, two new, more physiologically oriented approaches were introduced. The first is based on local administration of recombinant tissue plasminogen activator<sup>5</sup> and the second on the use of surface active material.<sup>6</sup> In the present article we would like to discuss the problem of postirradiation intraabdominal adhesions in the light of the use of surface active materials.

# Postirradiation intraabdominal adhesions

Chronic postirradiation enteritis is most often a disease of middle aged women treated by irradiation for gynecologic carcinoma.<sup>7</sup> Less frequently it is observed in older men treated for prostatic cancer<sup>8</sup> and in younger men treated for malignant testicular tumors.<sup>9</sup> The latent period between irradiation and appearance of the first symptoms of irradiation enteritis is very variable: it ranges form half a year to 31 years, being about 6 years on average.<sup>10</sup>

In the past, little attention was devoted to the problem of postirradiation adhesions. The bulk of the research on chronic postirradiation enteritis was centred on the mucosa or the bowel wall. Thus, chronic postirradiation enteritis was found to appear as a mucosal damage (ulcerations and fissures), or as a generalised fibrosis of the bowel wall with special emphasis on the submucous layer, and as a damage of the vessels resembling those at atherosclerosis.<sup>10</sup> The injury is frequently localised as jejunitis, ileitis or proctitis, but most often it is a combination of all previously mentioned localisations. It is expressed clinically as malabsorption, or bowel obstruction, which is mainly due to intraabdominal adhesions, or as bleeding on the stool.

At operation, the surgeon is faced by a difficult situation. At the beginning of surgery, slow and meticulous adhesiolysis is done; afterwards, resection and anastomosis of the bowel are performed if necessary. After this first intervention there are frequently recurrences of adhesive ileus. In these cases, subsequent sur-

Correspondence to: Marko Snoj MD, PhD, Institute of Oncology, Department of Surgery, Zaloška 2, 61105 Ljubljana, Slovenia.

gery is even more difficult than the first one and carries significant mortality. Therefore it would be highly warranted to prevent the recurrence of adhesive ileus.

Recently, it was realised that the studying of bowel serosa is the key to the solution of the problem of adhesive obstruction after irradiation.<sup>3</sup> Thus, it was observed in a rat model that intraabdominal adhesions began to from two months after abdominal irradiation with a single-dose of 13.5 - 17.5 Gy. They were associated with a concurrent serosal destruction. Postirradiation adhesions were even more expressed when there was inflammation present, or after a surgical procedure in this region.<sup>11</sup>

# Surface active materials

Surface active materials are present in the peritoneal fluid in a concentration from 11 to 25 mg/L. Its relative concentration is: 81 % phosphatidylcholine, 5% lysophosphatidylcholines, 6.5% sphyngomyelines, 3.5% phosphatidylinositols and 4% phosphatidyletanolamines.<sup>12</sup> It was postulated that phospholipid adheres to both parietal and visceral peritoneal surfaces and is held in place by the attraction of the positive charge of choline head to the negative charge of peritoneal surface. To the cavity long-chain fatty acids are presented and interacting with their counterparts from opposing side provide lubrication.<sup>12</sup>

We have found out in animal experiments that the surface active materials effectively prevent adhesions after surgery,<sup>6</sup> adhesions after intestinal anastomosis<sup>13</sup> and those after bacterial peritonitis.<sup>14</sup> Therefore they could be instilled in the peritoneal cavity after the adhesiolysis in postirradiation adhesive ileus.

# Postirradiation adhesions prevention by surface active materials

Surface active materials efficiently prevent intraabdominal adhesion formation only when instilled intraperitoneally, but not when applied intravenously.<sup>6</sup> When applied intraperitoneally, special attention should be paid to possible formation of intestinal anastomosis, since too high a dosis could lead to anastomotic dehiscence and peritonitis.<sup>13</sup>

The next question applies to the appropriate timing of surface active material application. Thus, application after irradiation does not seem wise since only about 5 % of patients later develop chronic irradiation enteritis. It seems much more possible to use them after the adhesiolysis for adhesive obstruction. In this case they could be instilled intraperitoneally at the end of the operation. This would be in line with experimental evidence that single dose of surface active material at the end of operation is as efficient as three doses in three consecutive days.<sup>13</sup>

It seems that surface active materials could play an important role in postirradiation adhesion prevention. Therefore, they bring the new light of hope for patients with this grave and often fatal disease.

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# Notices

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

#### Role of radiotherapy in the management of cancer

The ESTRO teaching course will take place in Prague, Czecho-Slovakia, *October 3–7*, *1993*.

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

#### **Basic clinical radiobiology**

The ESTRO teaching course will take place in Tours, France, October, 1993.

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## Psycho-oncology

The ESO training course "5<sup>th</sup> psycho-oncology update: psychosocial factors in morbidity and mortality" will take place in New York, USA, *October 2–4, 1993.* 

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# Publishing

The ESO training course for the Balkans and Middle East titled "the scientific writer, editor, referee or publisher" will take place in Athens, Greece, *October* 6–9, 1993.

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# Therapeutic radiology and oncology

The annual meeting of the American Society for Therapeutic Radiology and Oncology (ASTRO) will be held in New Orleans, L. A., USA, *October 11–15*, *1993*.

#### Lymphomas

The ESO training course for the Balkans and Middle East will be held in Athens, Greece, *October 18–22*, 1993.

Contact European School of Oncology – Athens Office, 2 Adrianiu St. & Papada ST., 118 25 Athens, Greece; or call + 30 1 6496 620. Fax: + 30 1 6924 372.

#### **Cancer clinical trials**

The ESO training course jointly organised with EORTC will take place in . . ., October 18–22, 1993.

Contact European School of Oncology – Brussels Office, Avenue Mounier, 83, 1200 Brussels; or call + 32 2 7724 621. Fax: + 32 2 7726 233.

#### **Growth factors**

The ESO seminar "Growth factors: from basic science to the clinic" will be offered in Venice, Italy, *October* 19–21, 1993.

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

### **Radiation oncology**

The Annual Meeting of the Austrian Society for. Radiation Oncology, Radiobiology and Medical Radiophysics will be held in Linz, Austria, *October* 23–24, 1993. Contact Dr. J. Hammer, Barmherzige Schwestern, Linz, Austria; or call +43 732 7677 ext. 7320. Fax: +43 732 7677 ext. 7200.

# Clinical oncology & cancer nursing

The 7<sup>th</sup> European conference will take place in Jerusalem, Israel, *November 13–19, 1993.* 

Contact FECS Secretariat, ECCO-7, Dept of Radiotherapy, University Hospital St Rafael, B-3000 Leuven, Belgium; or call + 32 16 33-64-13. Fax: + 32 16 33 64 28.

# The 12<sup>th</sup> annual ESTRO meeting

The meeting will be held during ECCO-7 in Jerusalem, Israel, November 13–19, 1993.

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

# Cancer

The "11<sup>th</sup> Asia Pacific Cancer Conference will be offered in Bangkok, Thailand, *November 16–19, 1993*.

Contact Phisit phanthumachinda, Oncological Society of Thailand, 5<sup>th</sup> Floor, National Cancer Institute, Rama VI Rd., Bangkok, Thailand 10400. Fax: + 66 2 24 79 428.

#### Radiology

The **79**<sup>th</sup> Scientific Assembly and Annual Meeting of the Radiological Society of North America (RSNA) will take place in Chicago, USA, *November 28 to December 3, 1993.* 

Contact the RSNA Secretariat 2021 Sprong Road, Ste. 600, Oak Brook, IL 60521, USA; or call 708 571 2670. Fax: 708 571 7837.

# Acknowledgment

Unit of Nuclear Medicine of the Institute of Oncology, Ljubljana, Slovenia, is very grateful to Professor Doctor Bojan Varl from Ljubljana, Slovenia, and to Professor Doctor Otto Eber from Graz, Austria, for their gift – Medical isotope spectrometer MIS 002/50 (BITT NUCLEAR) with computer and printer support.

# FIRST ANNOUNCEMENT

# 2<sup>nd</sup> Central European Conference on Lung Cancer

# LUNG CANCER – BIOLOGY AND CLINICAL ASPECTS LJUBLJANA – SLOVENIA

# April 13–16, 1994

Sponsored by

# The International Association for the Study of Lung Cancer

Organized by

# Slovenian Surgical Association Slovenian Respiratory Society Slovenian Cancerologic Association

# WELCOME MESSAGE

Dear Colleagues,

Slovenia has the honour to host and organize the 2<sup>nd</sup> Central European Conference on Lung Cancer under the auspices of the International Organization for the Study of Lung Cancer. The Conference will take place in Ljubljana on April 13 to 16, 1994.

The aim of the meeting is to bring together in a stimulating and agreeable environment researches and clinicians from Europe concerned with various problems of lung cancer. Plenary lectures given by invited speakers from distinguished medical schools will throw light on the state of the art in all aspects of lung cancer. Specialists in different disciplines will report their experience and results. Colleagues involved in the diagnosis, therapy and epidemiology of the disease, as well as those working in biology, pathology and other related fields are invited to participate.

The Conference will be held in a modern Congress centre in Ljubljana, the capital of our young independent Republic of Slovenia. The Organizing committee will spare no effort to make your attendance professionally and socially rewarding. Our objectives are to provide you with an opportunity to update your knowledge, present the results of your research and clinical work, and meet colleagues in a pleasant, relaxed atmosphere.

We hope to welcome you to our Conference in Ljubljana and look forward to showing you our lovely country, situated in the south of Central Europe, on the sunny side of the Alps, touching the Mediterranean.

J. Orel Chairman of the Organizing Committee

# **Organizing Committee**

Chairman J. Orel Secretary M. Bitenc Treasurer M. Sok Members B. Hrabar V. Kovač T. Rott F. Šifrer S. Vidmar

# **Main Topics**

Epidemiology of lung cancer Biological aspects Immunological aspects Experimental aspects and research Screening methods Staging of lung cancer Pathology and cytology Early detection Diagnostic methods Diagnostic imaging Endoscopic techniques Invasive diagnostic methods Laser endoscopy in lunger cancer Evaluation of patient for surgery Surgery of NSCLC Radiation therapy of NSCLC Chemotherapy of NSCLC Multimodality treatment of NSCLC Immunotherapy of NSCLC Brachytherapy of lung cancer Chemotherapy of SCLC Radiation therapy of SCLC Indications for surgery of SCLC Treatment of secondary lung cancer Surgery for lung metastases Therapy of lung cancer in the elderly Quality of life after surgery Prevention of lung cancer

# **General Information**

Conference Dates Conference Venue

Conference Language Secretariat

**Conference** Organizers

April 13-16, 1994

CANKARJEV DOM Cultural and Congress Centre Prešernova 10 61000 Ljubljana, Slovenia

English

J. Orel (Chairman) M. Bitenc (Secretary) Department of Thoracic Surgery Medical Centre Zaloška 7 61105 Ljubljana, Slovenia Tel.: + 38 61 317 582 Fax: + 38 61 116 006 Telex: 062 31499 Yuklicen

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For more information please do not hesitate to contact

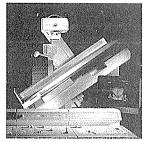
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# **IMPORTANT DATES**

Submission of abstracts: 15th July 1993 Notification of acceptance: 15th September 1993 Early registration: 15th October 1993

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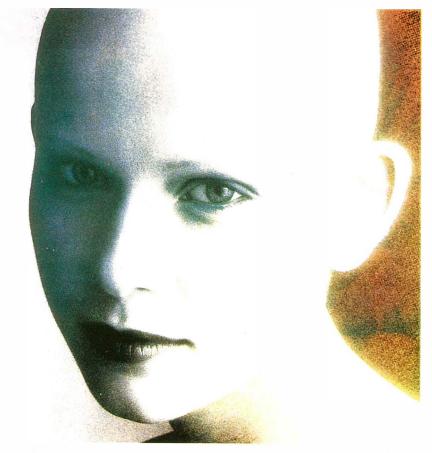
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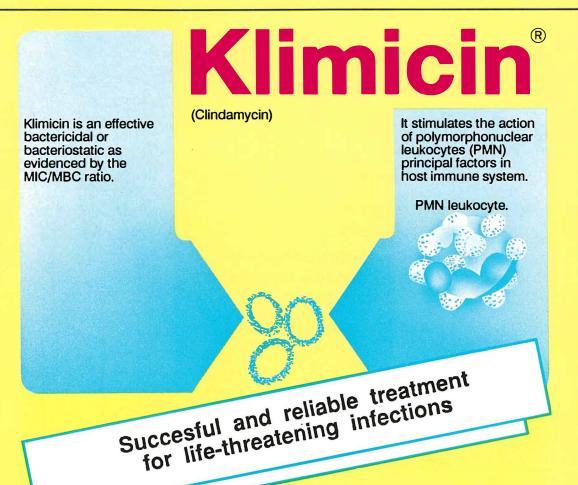
Gastro-intestinal disturbances, muscle and/or connective tissue pains, photosensitivity reactions, neurologic disturbances (headache, insomnia), and thrombocytopenia (at doses of 1600 mg daily) may occur.

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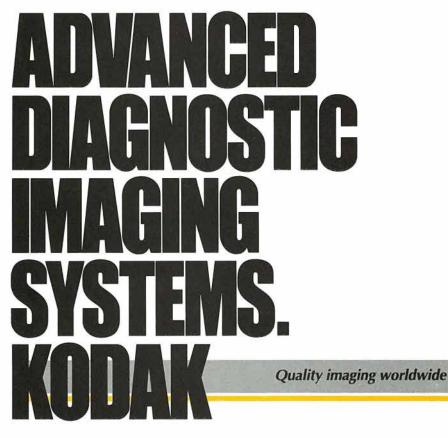
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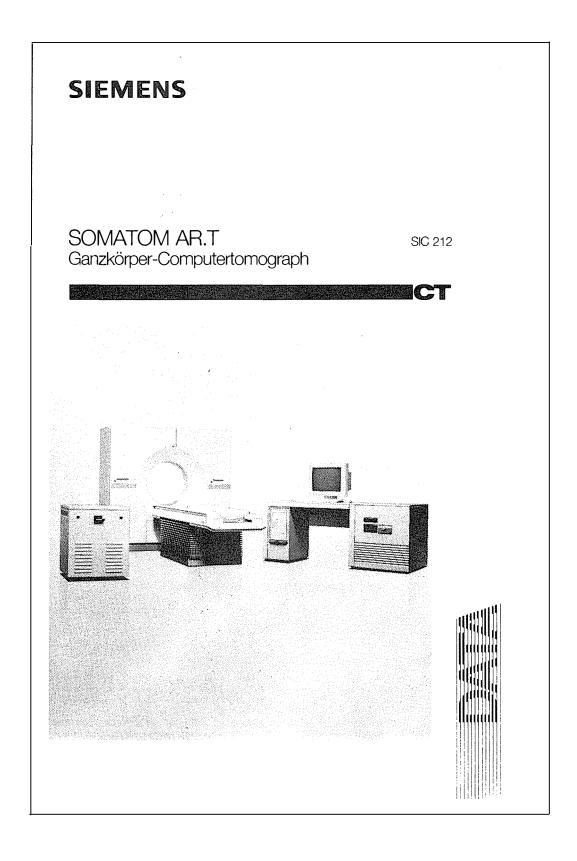
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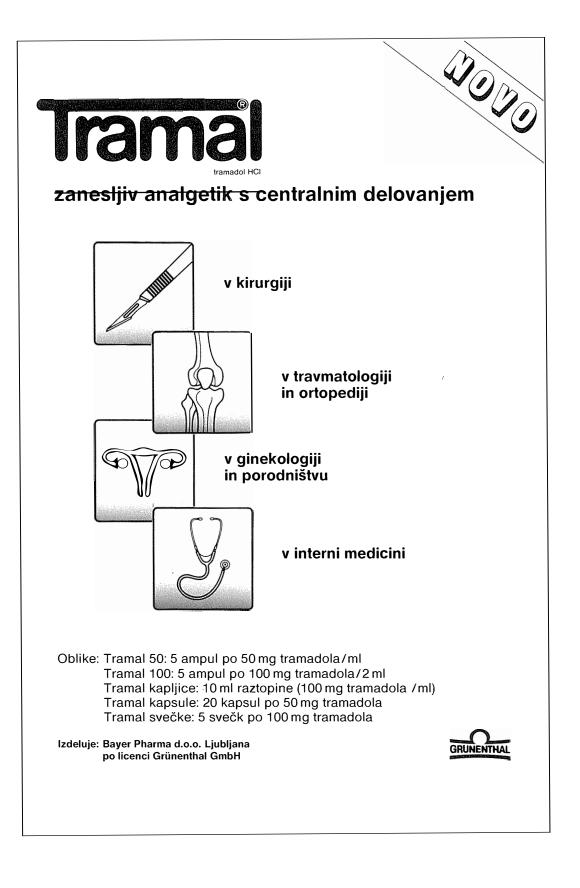
ampicilin, zaščiten s sulbaktamom – zato odporer proti delovanju beta laktamaz	١
razširja antibakterijsko delovanje ampicilina na po Gramu pozitivne bakterije, ki izločajo penicilinazo, na po Gramu negativne in anaerobne bakterije, vključno Bacteroides fragilis, ter tako povečuje klinično uporabnost in učinkovitost ampici	
visoko učinkovit v ambulantnem in bolnišničnem zdravljenju infekcij zgornjih in spodnjih dihal, sečil, rodil, kože ter mehkih tkiv	
možnost oralne in parenteralne uporabe	
izključuje potrebo po kombiniranem zdravljenju	
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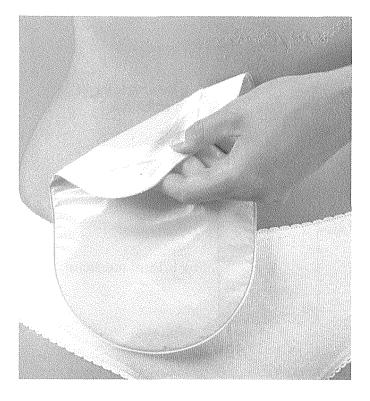
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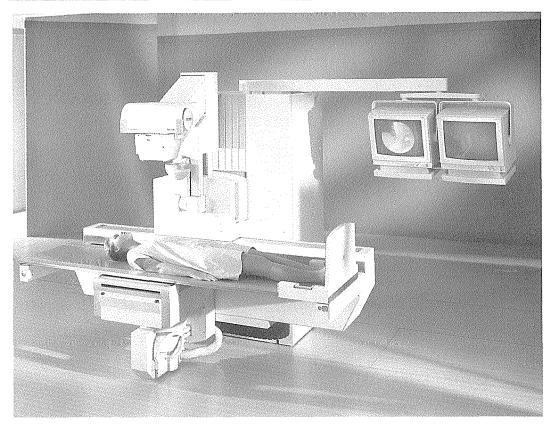
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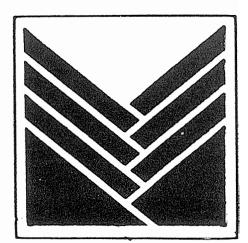
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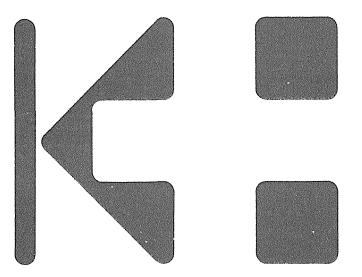
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Manuscripts written in English should be sent to the Editorial Office: Radiology and Oncology, Institute of Oncology, Vrazov trg 4, 61000 Ljubljana, Slovenia; Phone; +3861314970; Fax: +3861329177.

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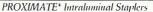
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