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# RADIOLOGIA IUGOSLAVICA

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LJUBLJANA

Radiol Iugosl January – March, 1991;25:1-90.


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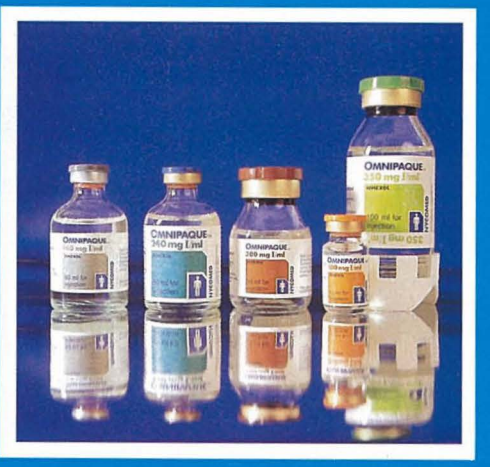


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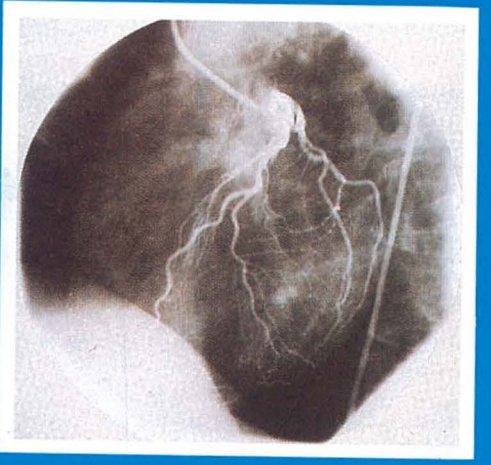

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# *BRALCEM, SODELAVCEM*

S to številko pričenjamo petindvajseti (in jubilejni) letnik naše revije. Ker smo o prvih dvajsetih letnikih že poročali (Radiol Iugosl 1988; 22: 221-4), bomo tokrat predstavili le opravljeno delo v zadnjih štirih letih oz. letnikih, in nakazali nadaljnji razvoj revije.

V štirih letnikih 1987–1990 je izšlo 18 številk, od teh 16 rednih in dve dodatni (leta 1987 številka s prispevki IV. jugoslovanskega kongresa nuklearne medicine in leta 1988 številka ob proslavi 90 let radiologije v Bosni in Hercegovini).

V osemnajstih številkah je bilo stiskano 2071 strani, v posameznem letniku povprečno 517 strani. Posamezna številka je obsegala povprečno 115 strani. Največ strani je bilo stiskano leta 1987 in to 652 strani, leta 1988 546, leta 1989 436 in leta 1990 437 strani.

Objavljenih je bilo 365 člankov, od katerih so jih 339 (92,9%) prispevali jugoslovanski avtorji. Tuji avtorji so objavili 26 (7,1%) člankov. Število objavljenih člankov iz republik, AP, VMA, inozemstva, članki v angleščini – po letnikih, je prikazano v tabeli 1. Čeprav število objavljenih člankov samo po sebi ne pomeni večje kvalitete, nam številčni prikaz vseeno omogoča vpogled v delovanje sodelavcev in ustanov. Največ objavljenih člankov je bilo iz Hrvatske, sledijo Slovenija, Bosna in Hercegovina, Srbija – ostali so prispevali le manjše število člankov.

Pomemben delež predstavljajo v angleščini pisani članki (79 – 21,6%) katerih število narašča, in članki inozemskih avtorjev.

Iz leta v leto upada število objav iz Bosne in Hercegovine, Makedonije, Srbije, VMA in Vojvodine, medtem ko število objav iz Hrvatske in Slovenije, kljub nihanjem v letnikih, ostaja na enakem nivoju. Vse kaže, da gospodarska in politična gibanja v Jugoslaviji vplivajo tudi na medicino, saj smo v letih 1964–1987 objavili okoli 50% člankov avtorjev s teh področij.

Razporeditev objavljenih člankov po stroki in letnikih objave je prikazana v tabeli 2. Največ člankov (93 – 25,5%) je iz rentgenske diagnostike in nuklearne medicine (88 – 24,1%), sledijo članki iz področja CT – UZ – MR (65 – 17,8%) ter članki iz drugih področij, ki jih objavlja revija. Opazno je zmanjševanje objav iz nuklearne medicine ter porast števila prispevkov iz področij CT-UZ-MR in onkologije-radioterapije. Vzrok upadanja nuklearnih člankov je verjetno v tem, da v zadnjih letih nismo tiskali nuklearnih zbornikov, medtem ko je dvig objav iz področij CT-UZ-MR posledica uvajanja novih tehnologij. Podobno velja za onkologijo-radioterapijo, vendar moramo pri tem upoštevati širino poglavja.

Razvoju znanosti in izboljšanju delovnih pogojev pri nas bo sledila tudi naša revija. V tiskanje bomo sprejeli manjše število in to le kvalitetnih prispevkov, saj zaradi napredka znanosti in informatike ni opravičeno objavljanje člankov brez pričakovanega mednarodnega odmeva. Zaradi tega bodo imeli prednost v angleščini pisani članki, s čimer bomo rezultatom raziskav, avtorjem in reviji omogočil vstop v še druge sekundarne biomedicinske publikacije.

Ob 25. letniku smo si uredniki s sodelovanjem obeh predsedstev zadali nelahko nalogo, da izdamo posebno, jubilejno publikacijo (knjigo) v angleščini, o kateri smo sproti obveščali v naših rednih številkah. Dosedanji potek dela je vzpodbuden, tako pri zbiranju sodelavcev kot pri organizacijskem delu.

S knjigo želimo bolje predstaviti dosežke naših avtorjev, pridobiti k stalnemu sodelovanju inozemske avtorje ter povečati število naročnikov doma in v inozemstvu. Knjiga bo izšla koncem leta 1991 in bo vsebovala predvsem pregledne, revijalne članke domačih in vabljenih tujih avtorjev s področij, ki jih obravnava revija. Pri izdaji knjige pričakujemo sodelovanje in pomoč posameznikov in vseh jugoslovanskih radioloških, nuklearno-medicinskih in onkoloških ustanov.

Kot v vseh letih izdajanja revije, je tudi v zadnjih štirih letih delo v uredništvu potekalo vzorno in brez zapletov, dobro smo sodelovali z avtorji, recenzenti in mnogimi ustanovami, ki so podprle naša prizadevanja. Uredniki se zahvaljujemo Onkološkemu inštitutu v Ljubljani in drugim ustanovam v Jugoslaviji, ki so omogočili, da je revija redno in uspešno izhajala.

Tabela 1 – Objavljeni članki iz republik, AP, VMA, inozemstva, članki v angleščini – po letnikih 1987–1990

| | 1987 | 1988 | 1989 | 1990 | SKUPAJ | % |
|---|---|---|---|---|---|---|
| BiH | 11 | 25 | 11 | 7 | 54 | 14,8 |
| Črna gora | 0 | 0 | 0 | 0 | 0 | 0 |
| Hrvatska | 47 | 34 | 24 | 32 | 137 | 37,5 |
| Kosovo | 0 | 0 | 0 | 0 | 0 | 0 |
| Makedonija | 4 | 1 | 0 | 0 | 5 | 1,4 |
| Slovenija | 18 | 8 | 19 | 22 | 67 | 18,4 |
| Srbija | 22 | 14 | 12 | 6 | 54 | 14,8 |
| Vojvodina | 9 | 1 | 1 | 2 | 13 | 3,5 |
| VMA | 5 | 0 | 4 | 0 | 9 | 2,5 |
| Inozemstvo | 3 | 9 | 1 | 13 | 26 | 7,1 |
| S k u p a j | 119 | 92 | 72 | 82 | 265 | 100,0 |
| Članki v angleščini | 10 | 17 | 20 | 32 | 79 | 21,6 |

Tabela 2 – Objavljena dela po področjih in letnikih 1987–1990

| POGLAVJE | LETNIK | | | | Število objav | % |
|---|---|---|---|---|---|---|
| | 1987 | 1988 | 1989 | 1990 | | |
| Rentgenska diagnostika | 31 | 27 | 17 | 18 | 93 | 25,5 |
| Nuklearna medicina | 51 | 16 | 11 | 10 | 88 | 24,1 |
| CT/UZ/MR | 9 | 16 | 15 | 25 | 65 | 17,8 |
| Onkologija-radioterapija | 4 | 6 | 11 | 16 | 37 | 10,1 |
| Interventna radiologija | 9 | 0 | 5 | 3 | 17 | 4,7 |
| Radiofizika | 4 | 8 | 0 | 3 | 15 | 4,1 |
| Radiobiologija | 1 | 3 | 6 | 0 | 10 | 2,7 |
| Eksperimentalna onkologija | 0 | 0 | 2 | 5 | 7 | 1,9 |
| Zaščita pred sevanji | 1 | 1 | 1 | 0 | 3 | 0,8 |
| Epidemiologija | 0 | 1 | 0 | 1 | 2 | 0,6 |
| Ekologija | 0 | 0 | 0 | 1 | 1 | 0,3 |
| Ostalo (projekti, zgodovina, medicine, bibliotekarstvo, nerazporejeno) | 9 | 14 | 4 | 0 | 27 | 7,4 |
| Skupaj | 119 | 92 | 72 | 82 | 365 | 100,0 |

Po dolgoletnem urednikovanju je svoje delo v uredništvu predal mlajšim kolegom prof. dr. Stojan Plesničar, soustanovitelj naše revije. Vseh 27 let je bil urednik, v letih 1982–1986 tudi glavni in odgovorni urednik. S svojo prizadevnostjo je bil vzgled in potrpežljiv učitelj vsem, ki smo se kasneje vključili v delo uredništva. V premnogih sproščenih pogovorih nas je prepričeval o pomenu tiskane besede in o vrednosti večkrat nelahkega dela, kateremu smo se predali novi uredniki. Z delom in optimizmom tudi v najtežjih trenutkih, je bistveno pripomogel k obstoju in napredku revije. Prof. dr. Stojanu Plesničarju se za opravljeno delo zahvaljujemo sedanji uredniki, ki z nadaljnjim delom uresničujemo marsikatero njegovo, pred leti še neuresničljivo zamisel.

Za 27 let trajajoče požrtvovalno delo, ki je često presegalo prostovoljni pristop, se zahvaljujemo tajnici uredništva Milici Harisch in knjigovodkinji Betki Savski. Brez njunega pomembnega prispevka revija danes zagotovo ne bi bila takšna kot je.

Spremenjena gospodarska in politična situacija v Jugoslaviji bo bržkone vplivala na strokovni in ekonomski položaj revije. Kljub temu, z upanjem, da so zdravstveni delavci in ustanove le nad vsakodnevnimi tegobami našega časa, pričenjamo 25. in jubilejni letnik revije in vabimo k nadaljnjemu sodelovanju.

Dr. Tomaž Benulič,
glavni in odgovorni urednik

THE INSTITUTE OF ONCOLOGY, LJUBLJANA

# THE ROLE OF RADIOLOGIST IN VERIFICATION OF MAMMOGRAPHICALLY SUSPICIOUS LESIONS FOR BREAST CARCINOMA

Us J

**Abstract** – The role of radiologist in the diagnosis of minimal radiographically visible changes in the breast, suspicious for breast cancer, is presented. The author believes that stereotactic aspiration biopsy is unable to provide a relaible explanation of mammographically evidenced changes in the breast. Accordingly, a histologic verification of such changes is considered indispensable. The role of radiologist is, therefore, to locate the change in the breast, as well as to help the surgeon in assessment of the outcome of surgery. Using specimen mamography, he assists the pathologist in defining the most suitable site for histologic sample taking.

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**Key words:** breast neoplasms, mammography, radiologist

**Review paper**

**Radiol Iugosl** 1991; 25:1-4.

**Introduction** – Mammography is undoubtedly the diagnostic method which helps us to detect breast cancer in the earliest stage of its development. Any changes in the breast structure such as clustered microcalcinations (in groups of 5 or more) and tiny stellate formations, appearing either separately or combined with each other, should be microscopically verified as they may predict a rise of breast cancer. No other presently available diagnostic method (clinical examination, transillumination, ultrasonography, thermography and others) has the potential of detecting such changes. Those evidenced by mammography, should be surgically removed and morphologically classified. The diagnosis of breast cancer should be morphologically confirmed.

Breast cancer can be morphologically confirmed by the use of cytological and/or histological methods. The most simple of them is fine-needle aspiration biopsy (AB) which can explain a great majority of clinically evident breast tumors. AB, however, is not successful in clinically ocult lesions, as the needle point used for AB can collect only the cells from its immediate surroundings. Thus in the cases when the needle point lies outside the suspicious area, only cells from lesion surroundings can be obtained, which are not always diagnostically relevant. The results obtained on AB can be false negative. When suspicion for breast cancer based on mamographical findings cannot be confirmed by cytological evidence of cancer cells, the breast lesion should be surgically removed for histologic examination.

Considering the above facts, the so-called »mammogram-based aspiration biopsy« does not make sense. The method is based on speculation that the cytologist can use mammography for positioning the site of AB. But, as a matter of fact, this appears reasonable only for aspiration biopsy of tumors inaccessible to clinical examination owing to large breasts, whereas unpalpable, only mammographically detectable lesions cannot be explained by this method. The latter can be most effectively explained by localization. The breast lesion is localized by means of wire with the tip in form of a hook. This method was first described by Frank in 1976 (1) and since then it has undergone several modifications so abroad as well as in our country (2). In 1977, Bolmgren (3) brought up the possibility of stereotactic AB of non-palpable breast lesions. A special computer-guided X-ray unit was developed which enabled localization of AB-detectable changes with ± 1 mm accuracy. When the lesion was found to

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be of malignant nature by stereotactic AB, it was localized (4) for surgical removal (5). In the cases when the lesion could not be sufficiently explained on AB, it also had to be localized to enable surgical sample taking for further diagnostic procedures (6). Evans (7) is in favor of stereotactic device believing that the use of this equipment facilitates localization of breast lesions.

**Our own experience** – At the Institute of Oncology in Ljubljana an attempt has been made to develop a device for stereotactic aspiration biopsy. According to a hypothesis in our study, the stereotactic method was hoped to save breast surgery in the cases when a benign nature of breast lesion would have been ascertained by stereotactic AB.

A prototype of such a device was worked out (Figure 1) based on the presupposition that the breast was of semi-lobular shape which enabled to determine the site and depth of breast lesion by the help of stereometry and coordinate system. The method was too rough and therefore unsuitable for practical use. Another prototype was produced in collaboration with TIK Kobarid company (8) (Figure 2). This apparatus used the same principle as Swedish TRC stereotactic device. X-ray geometry and the depth of breast lesion were calculated according to the following formula:

$$Z = \frac{r^*\cos\alpha}{r^*\sin\alpha + X_2} * \left[ X_2 - \frac{r^*\sin\alpha^* (X_1 + X_2)}{2^*r^*\sin\alpha - X_1 + X_2} \right]$$

where Z was the depth, r – focus-film distance, $\alpha$-angle of entering X-rays, $X_1$ – shadow decline to the left. $X_2$ – shadow decline to the right.

A program for ZX SPECTRUM computer was worked out. The experiments for determination of depth (Z) on a paraffin phantom with tiny metal grains of 1 mm diameter inserted at a previously determined depth gave encouraging results. The depth could be determined with 1 mm accuracy. Two opposing radiograms of the phantom were taken at the angle of 30°. Shadow decline in mm was determined on radiograms by means of X-ray film being placed over a radiopaque measure grid. After inserting the values for angle alpha, X1 and X2, the position (Z) of the shadow was calculated by the computer.

X-ray imaging of the breast was not successful, however, due to eccentrically mounted X-ray tube which rendered radiography of the breast impossible.

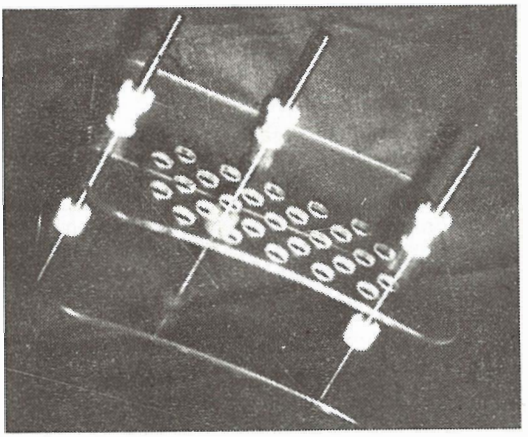

Fig. 1 – The first prototype of a device for stereotactic biopsy of the breast

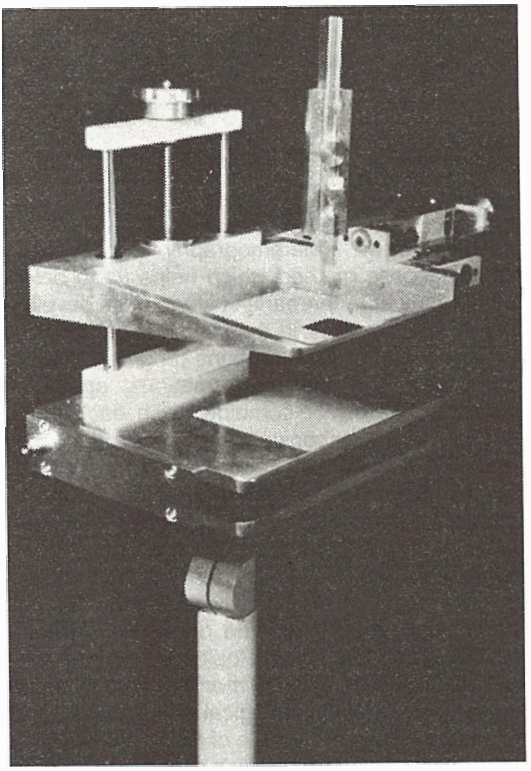

Fig. 2 – A prototype of stereotactic device for breast biopsy produced by TIK Kobarid Company

Considering that stereotactic biopsy of breast lesions was not feasible, we attemped to perform the investigation on a tissue specimen removed on surgery. The search of a representative speci-

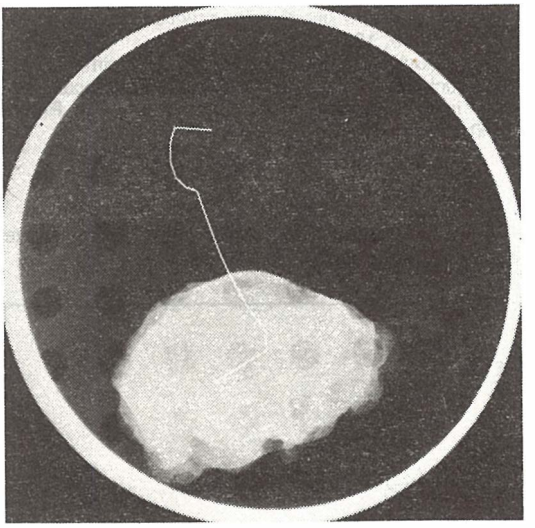

Fig. 3 – Specimen mammography

men in the removed breast tissue is a demanding task for the pathologist. If in the case of a breast cancer the tissue specimen is non-representative, the morphologic investigation of frozen section will give false results. Breast cancer can be confirmed only by definitive histologic findings. Therefore, the stereotactic method was aimed at facilitating the pathologist's work and saving the patient from repeated surgery. For this purpose we used a special box with perforated top plate; the holes were marked with a radiopaque grid. The removed breast tissue was placed into the box and radiographed. The site of representative sample taking was marked with a needle inserted through the hole in the box top (9). The method proved very reliable, though it required close collaboration between the radiologist, surgeon and pathologist (Figure 3).

The technique was further improved in a way that the stereotactic box was replaced by a paraffin-filled petri dish (10). The surgeon placed the severed part of the breast onto hardened paraffin. Petri dish containing the surgical specimen was put into a plastic bag and sent to the Department of Diagnostic Radiology for specimen X-ray examination, so-called sample-mammography. Radiography was done using a radiopaque grid. After having established the coordinates, a needle was inserted through the specimen into paraffin, thus fixing the tissue to the bottom. This helped the pathologist to find the optimum sample taking site quickly and easily.

Undoubtedly, the localization of such changes in a specimen is very important (9) as it improves the accuracy of frozen section histology and, consequently, saves the patient from event repeated surgery. Selfevidently, this enables the surgeon to perform tumor removal and local lymph node dissection in one and the same session.

**Conclusion** – The complicated problem of minimum breast cancer diagnosis cannot be adequately solved by stereotactic AB of the breast. Final diagnosis is based on the pathologist's assessment of the surgically removed breast tissue. However, the determination of representative sample taking site requires collaboration of a radiologist who performs sample-mammography and locates the lesion site with a needle. In finding the representative sample taking site the pathologist is assisted by a sample-mammograph and the marked specimen.

**Povzetek**

VLOGA RENTGENOLOGA PRI VERIFIKACIJI ZA RAK DOJKE SUMLJIVIH MAMOGRAFSKIH SPREMEMB

Avtor prikazuje vlogo rentgenologa v diagnostiki minimalnih, za raka mamografsko sumljivih sprememb v dojki. Avtor je mnenja, da je streotaktična aspiracijska biopsija določevanja narave, mamografsko ugotovljenih sprememb v dojki nezadostna. Po njegovem prepričanju je nujna histološkja verifikacija mamografsko ugotovljenih sprememb. Naloga rentgenologa je, da lokalizira spremembo v dojki, sodeluje s kirurgom pri ugotavljanju radikalnosti operativnega posega. Na osnovi preparat mamograma pa pomaga patologu do reprezentančnega mesta iz katerega patolog vzame tkivni vzorec za preiskavo.

**Acknowledgement** – The author wants to thank Prof. dr. R. Golouh, M. D, and J. Lamovec M. D. for their useful advice and collaboration.

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KLINIČKI BOLNIČKI CENTAR
ZAVOD ZA RADIOLOGIJU

# SISTEMNO–PORTALNE KOLATERALE KOD OKLUZIJE DONJE ŠUPLJE VENE

## SYSTEMIC–PORTAL COLLATERALS IN INFERIOR VENA CAVA OBSTRUCTION

Radanović B, Šimunić S, Oberman B

**Abstract** – Development of systemic-portal collaterals in three patients with inferior vena cava obstruction is reported. Depending on the level of the inferior vena cava obstruction of (and/or iliac veins), numerous systemic but rarely systemic-portal collaterals develop.

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**Key words:** vena cava inferior obstruction, collateral circulation

**Orig sci paper**

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**Uvod** – Čitav niz patoloških procesa može uzrokovati opstrukciju donje šuplje vene i ilijačnih vena. Ovisno o lokalizaciji i proširenosti opstrukcije dolazi do razvoja sistemno-sistemnih i sistemno-portalnih kolateralnih venskih puteva. Opstrukcija donje šuplje vene može biti lokalizirana u infrarenalnom, središnjem i gornjem dijelu. Kod infrarenalne opstrukcije mogu biti zahvaćene i ilijačne vene, a kod središnje, odnosno gornje lokalizacije mogu biti zahvaćene i hepatalne vene. Središnja opstrukcija sa zahvaćanjem renalnih vena najčešće je klinički praćena nefrotskim, a gornja je praćena Budd-Chiarijevim sindromom (1, 2, 3, 4).

U grupi sistemno-sistemnih venskih kolaterala glavnu ulogu ima centralni kolateralni krvotok preko vertebralnih venskih spletova, ascendentnih lumbalnih vena i sistema vene hemiazigos i azigos. Intermedijarne sistemno-sistemne kolateralne puteve predstavljaju ovarične i ureterične vene. Sistemno-sistemne kolaterale prednje trbušne stijenke predstavljaju superficijalna i donja epigastrična vena s donjom epigastričnom, torakoepigastričnom venom i venom toracikom internom.

Porto-sistemne kolaterale kod portalne hipertenzije redovito su prisutne u manjem ili većem opsegu. Sistemno-portalne kolaterale kod opstrukcije donje šuplje vene javljaju se izuzetno rijetko. Do sada je objavljeno relativno malo publikacija s prikazom sporadičnih slučajeva.

Sistemno-portalne kolaterale mogu se razviti kod opstrukcija donje šuplje vene u sva tri nivoa. Kod infrarenalne opstrukcije uključujući i ilijačne vene najčešće se razvijaju sistemno-portalne kolaterale preko zdjeličnih venskih spletova i rektalnih vena, odnosno donje mezenterične vene. Kod niskih oblika opstrukcije nešto rjeđe se razvijaju sistemno-portalni kolateralni putevi preko donjih epigastričnih i paraumbilakalnih vena, te umbilikalne vene. Ovarične i spermatične vene mogu razvojem kolaterala s venom kolikom sinistri također postati jedan vid sistemno-portalnih kolaterala.

Lumbalne, renalne i suprarenalne vene mogu kod srednje i visoke opstrukcije donje šuplje vene formirati sistemno-portalne kolateralne puteve prvenstveno preko gornje mezenterične vene, a rjeđe preko donje mezenterične vene (2, 3, 5, 6, 7, 8, 9, 10).

**Bolesnici i metode** – Kroz protekli trogodišnji period kod 28 bolesnika dijagnosticirali smo opstrukciju donje šuplje vene s različitim razvojem

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sistemno-sistemnih venskih kolaterala. Samo u tri bolesnika razvile su se sistemno-portalne kolaterale i prikazani su u rezultatima.

Patološki procesi koji su u naših bolesnika uzrokovali opstrukciju donje šuplje vene bili su: maligni renalni tumori (12), hepatomi (3), malignomi zdjelice (5) i retroperitonealni tumori (3), kongenitalna anomalija donje šuplje vene (1), nepoznata etiopatogeneza (4) bolesnika.

Flebografska obrada rađena je uni- ili bilateralnim transfemoralnim pristupom, a u 10 bolesnika prethodno je rađena i ascendentna flebografija donjih ekstremiteta.

**Rezultati** – Bolesnik A : M. N., 17-godišnji bolesnik primljen je na internističku obradu zbog recidivirajućih flebotromboza donjih ekstremiteta, te bolova u području zdjelice i donjeg abdomena.

Na učinjenom CT-u zdjelice i abdomena nađen je infiltrativni neoplastički proces presakralnog dijela zdjelice sa zahvaćanjem vaskularnih struktura zdjelice.

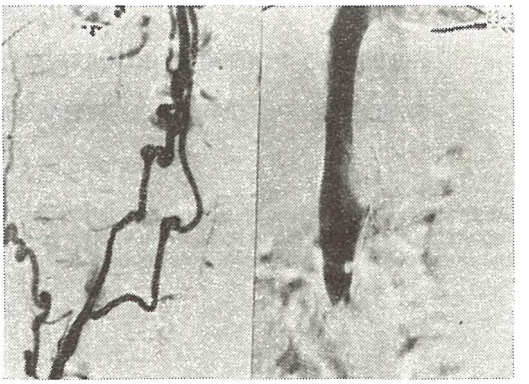
Bilateralnom ascendentnom flebografijom nađena je trombotička okluzija u srednjim trećinama femoralnih vena, a venska drenaža odvijala se preko površnih venskih spletova donjih ekstremiteta i prednje trbušne stijenke.

Direktnom punkcijom donje epigastrične vene na desnoj strani dobili smo prikaz tortuoznih venskih spletova prednje trbušne stijenke, koji dijelom anastomoziraju s torakoepigastričnim venama, a dijelom se kontrastna krv drenirala preko rekanalizirane široke umbilikalne vene s prikazom intrahepatalne portalne cirkulacije u lijevom režnju jetre (umbilikalna vena redovito se odvaja iz lijeve grane portalne vene, a iznimno iz portalne grane za desni režanj jetre) (Slika 1a, b; slika 2).

Flebografsku obradu sliva donje šuplje vene završili smo transkubitalnom i transkardijalnom flebografijom proksimalnog dijela donje šuplje vene, pri čemu smo dijagnosticirali infrarenalnu okluziju donje šuplje vene s nesmetanim utokom renalnih i hepatalnih vena.

Daljnji tok bolesti bio je karakteriziran brzom progresijom malignoma zdjelice, unatoč provedenom onkološkom liječenju. Patohistološki nalaz : Liposarkoma.

Bolesnik B : M. K, 43-godišnja bolesnica operirana je zbog karcinoma maternice, a u tri navrata provedena je iradijacija. Unatoč iradijacijskom liječenju dolazi do progresije osnovne bolesti, a uz to se na donjim ekstremitetima razvija i klinička slika bilateralne flebotromboze, nešto naglašenije na desnoj nozi.

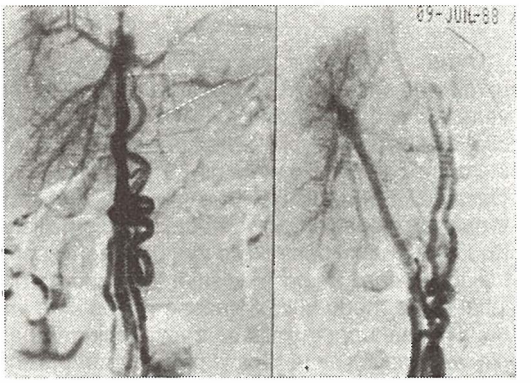


Slika 1 a, b – a) Flebografija donje epigastrične vene: tortuozan tok donje i superficijalne epigastrične vene

b) Transkubitalna flebografija donje šuplje vene: infrarenalna okluzija donje šuplje vene sa slobodnim utokom renalnih i hepatalnih vena

Fig. 1 a, b – a) Inferior epigastric vein phlebography: tortuous course of the inferior and superficial epigastric veins.

b) Transcubital phlebography of the inferior vena cava: subrenal vena cava occlusion with unobstructed renal and hepatic veins




Slika 2 – Flebografija donje epigastrične vene: tortuozan tok epigastričnih vena u gornjem dijelu s prikazom umbilikalne vene i intrahepatalne arborizacije portalne vene u lijevom jetrenom režnju

Fig. 2 – Inferior epigastric vein phlebography: tortuous epigastric veins in the superior part with demonstration of the umbilical vein and intrahepatic branches of the portal vein in the left hepatic lobe

Na učinjenoj flebografiji zdjelice i donje šuplje vene nađe se proširena lijeva ilijačna vena koja je okludirana neposredno ispred utoka u donju šuplju venu. Razvijene su opsežne sistemno-sistemne kolaterale putem centralnog venskog ko-

lateralnog krvotoka, koji od visine L-5 puni postokluzivni dio donje šuplje vene. U samoj zdjelici preko venskih kolaterala lijeve unutarnje ilijačne vene i rektalnih vena puni se široka vena mezenterika inferior, koja predstavlja hemodinamski značajan kolateralni sistemno-portalni put (Slika 3a, b; slika 4a, b).

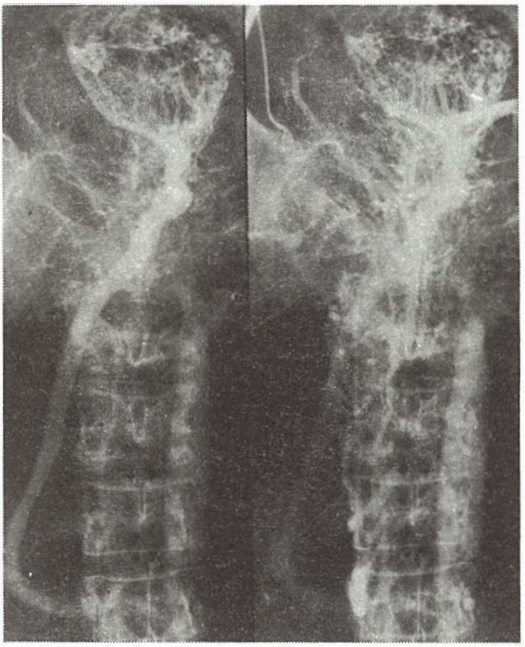
Progresija osnovne bolesti s metastazama u jetri i plućima odredila je daljnji tok bolesti, unatoč onkološkom liječenju.

Bolesnik C : Ž. M, 16-godišnji bolesnik dolazi radi flebografske obrade zbog proširenih površnih vena donjih ekstremiteta i prisutnih edema potkoljenica.

Bilateralna ascendentna flebografija pokazala je normalnu vensku hemodinamiku donjih ekstremiteta.

Bilateralnim transfemoralnim pristupom prikazane su umjereno proširene ilijačne vene, a u donjoj trećini donje šuplje vene nalazimo pseudoaneurizmatsko proširenje. Prema kranijalno je usmjeren filiformni kontrastni tračak koji odgovara rezidualnom lumenu donje šuplje vene, a pretežno lijevo paravertebralno dobro su razvijeni paravertebralni venski pleksusi. U kasnijoj fazi desno paravertebralno prikazuju se široki tortuozni venski spletovi koji dislociraju ureter i pijelon desnog bubrega. Kroz tortuozne vene cirkulacija je izrazito usporena. Tek u terminalnoj fazi flebografije uočava se izuzetno blijeda kontrastna opacifikacija gornjeg dijela vene mezenterike superior i vene porte (Slika 5 a, b, c).

Pretpostavku o kongenitalnoj anomaliji donje šuplje vene (aplazija suprarenalnog dijela donje

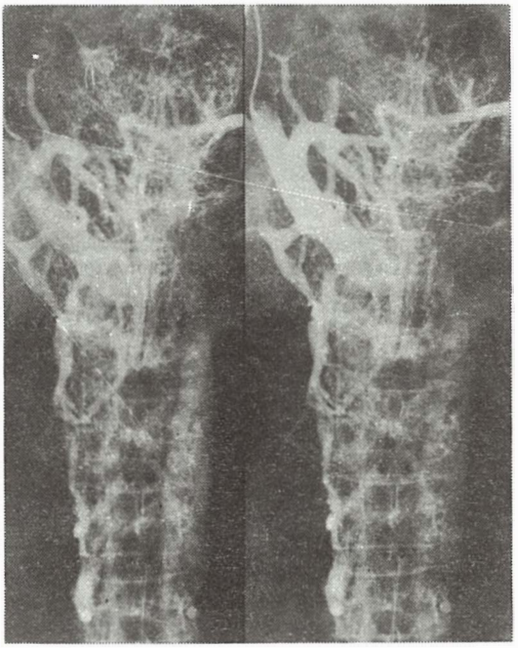


Slika 3 a, b – a) Lijevostrana zdjelična flebografija: proširena lijeva ilijačna vena s okluzijom u terminalnom dijelu i opsežne sistemno-sistemne kolaterale

b) Prikaz postokluzivnog dijela donje šuplje vene i centralnog vertebralnog venskog sistema

Fig. 3 a, b – a) Left pelvic phlebography: dillated left iliac vein with terminal occlusion and ample systemic collaterals

b) Revised part of the inferior vena cava and the central vertebral vein system is demonstrated

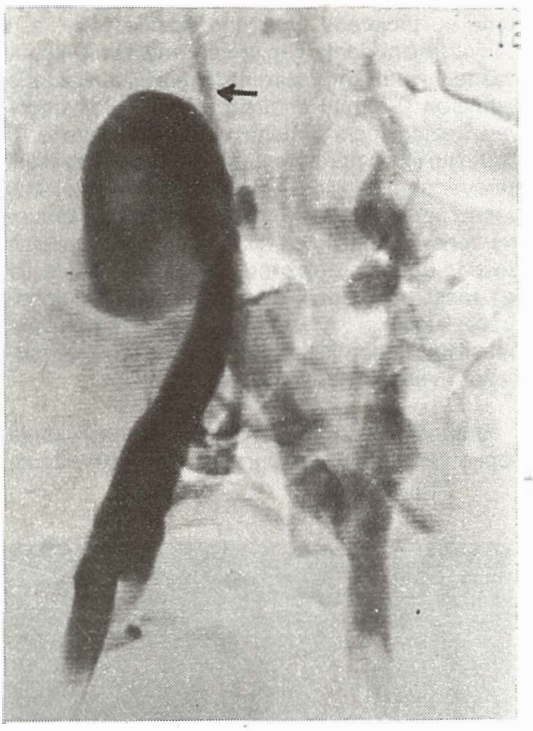


Slika 4 a, b – a) Sistemno-sistemne kolaterale centralnog kolateralnog venskog sustava uz početno punjenje rektalnih vena i donje mezenterične vene

b) Drenaža venske krvi preko donje mezenterične vene

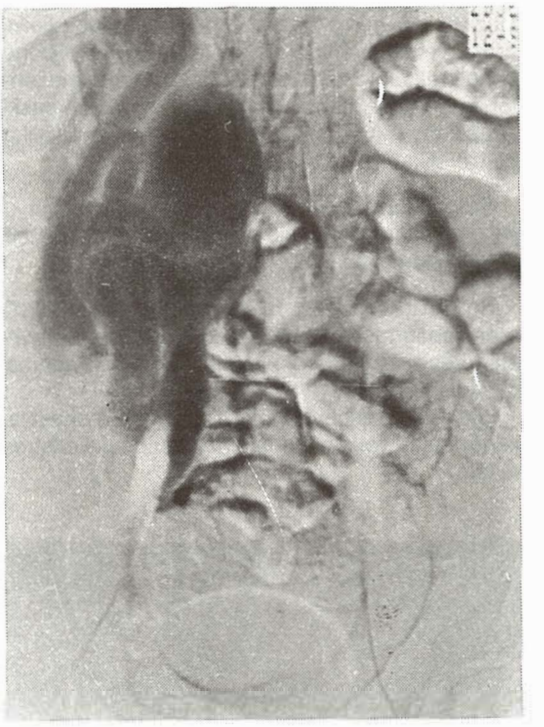
Fig. 4 a, b – a) Systemic collaterals of the central venous collateral system with initial filling of rectal veins and the inferior mesenteric vein

b) Venous blood drainage via the inferior mesenteric vein



Slika 5 a – Zdjelična flebografija: bilateralni prikaz ilijačnih vena s pseudoaneurizmatskim proširenjem početnog dijela donje šuplje vene (strelica pokazuje filiformno punjenje hipoplastičnog dijela donje šuplje vene)

Fig. 5 a – Pelvic phlebography: bilateral iliac veins demonstration with pseudoaneurysmatic dilatation of the initial portion of the inferior vena cava (arrow points to delicate filling of hypoplastic part of the inferior vena cava)



Slika 5 b – Opsežni tortuozni venski spletovi desne paravertebralne regije

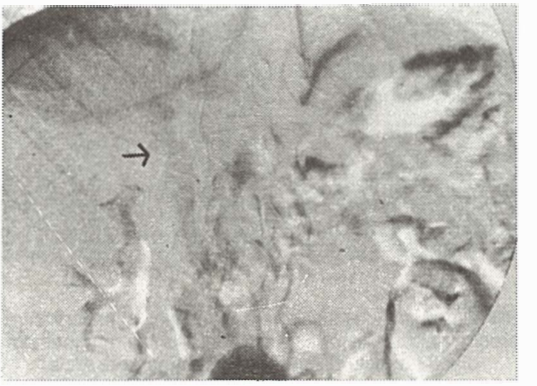
Fig. 5 b – Ample tortuous venous network of the right paravertebral region

šuplje vene) potvrdili smo angiokardiografskom obradom desnog srca pri kojoj nismo našli ušće donje šuplje vene u desnom atriju.

Nakon konzultacije nekoliko evropskih vaskularnih kliničkih centara odustalo se od operativnog rekonstruktivnog zahvata donje šuplje vene zbog izuzetno visokog operativnog rizika.

**Diskusija** – Prvi flebografski prikaz sistemno-portalnih kolaterala nakon ligature donje šuplje vene nalazimo objavljen u radu Gvozdanovića i suradnika 1957. U dva od ukupno trideset bolesnika u kojih je učinjena ligatura donje šuplje vene opisane su sistemno-portalne kolaterale (2).

Čitav niz autora u novije vrijeme prikazuje male serije ili pojedinačne slučajeve razvoja sistemno-portalnih kolaterala kod neoplastične i



Slika 5 c – Terminalna faza flebografskog pregleda pokazuje blijedi kontrastni prikaz završnog dijela gornje mezenterične vene i vene porte

Fig. 5 c – Final phase of phlebography shows a pale contrast demonstration of terminal part of the superior mesenteric and portal veins

posttrombotične opstrukcije donje šuplje vene (1, 4, 9, 11, 12, 13).

Ova disproporcija broja opstrukcija donje šuplje vene, koje predstavljaju relativno čestu angiološku problematiku i izuzetno rijetko prikazanih sistemno-portalnih kolaterala potaknula je Albrechtssona da potraži razlog takvom odnosu. On osim hemodinamskih razloga nalazi tome uzroke i u malim ukupnim količinama kontrastnog sredstva, te nedovoljne protrahiranosti flebografskog pregleda (1).

Ovu pretpostavku kod nekoliko prikazanih slučajeva potvrđuju Hipona i Gabriele koji su bilateralnim femoralnim aplikacijama 60 ml kontrastnog sredstva i protrahiranom metodom pregleda bitno poboljšali kvalitetu prikaza postojećih sistemno-portalnih kolaterala (9). Navedeni autori protrahiraju pregled na 60-120 sekundi nakon aplikacije kontrastnog sredstva. Mi smo u naših bolesnika zadnje snimke radili 30 sekundi poslije aplikacije kontrastnog sredstva i dobili zadovoljavajuće morfološke i hemodinamske prikaze.

Značajan korak naprijed i u ovom segmentu angiografske dijagnostike predstavlja digitalna suptrakcijska angiografija (DSA). Nasuprot značajnim povećanjima ukupne količine kontrastnog sredstva kod konvencionalnih radioloških metoda, kod DSA aplicira se svega 10-15 ml kontrastnog sredstva, a vizualizacija venskih kolateralnih puteva bitno je poboljšana (14, 15). U naša tri opisana bolesnika sa sistemno-portalnim kolateralama u dvoje je učinjena DSA.

**Zaključak** – Morfološka i hemodinamska analiza kolateralne venske cirkulacije kod opstrukcije donje šuplje vene praktički je isključivo prešla u domenu angioradiološke dijagnostike. Određene modifikacije konvencionalnih radioloških metoda, a osobito upotreba digitalne suptrakcijske angiografije, bitno su pridonijeli kvaliteti dijagnostičke analize.

Najčešći nastanak kolaterala kod opstrukcije donje šuplje vene su sistemno-sistemni venski putevi. U značajno manjem opsegu razvijaju se sistemno-portalne kolaterale, pri čemu vena porte ima centralnu integralnu ulogu pojedinih vidova sistemno-portalnih kolaterala.

**Sažetak**

Autori izvještavaju o nastajanju sistemno-portalnih kolaterala u tri bolesnika s opstrukcijom donje šuplje vene. Ovisno o nivou opstrukcije donje šuplje vene (i/ili ilijačnih vena) dolazi do razvoja brojnih sistemno-sistemnih, a tek rijetko sistemno-portalnih kolaterala.

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# DUODENALNI GENO–BULBARNI PROLAPS

## DUODENAL–FLEXURAL–BULBAR PROLAPSE

Goldner B[1], Šerić M[1], Bulajić M[2], Marković S[3], Dodić M [1]

**Abstract** – Authors describe intermittent prolapse of the superior duodenal flexure into a bulb which produces the appearance of a filling defect mimicking a smooth sharply delineated polypoid mass with a central ulceration or an ulcer with surrounding edema.
Coarcened circular mucosal surface pattern around flexural pseudotumor or false ulcer with changeability of a structural bulb feature, distinguish this entity from a real bulbar lesion.

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**Key words:** duodenal diseases-radiography, prolapse

**Profess paper**

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**Uvod** – Povremeni prolaps gornje fleksure duodenuma u bulbus je malo poznat rendgenološki entitet kome je u dosadašnjoj stručnoj literaturi posvećena neznatna pažnja (1), jer ga klasične rendgenološke knjige svetskih autora kao i udžbenička i monografska dela na našem jeziku ne pominju.

Promenljiva rendgenološka slika bulbusa u kome se smenjuju naizgled patomorfološke promene sa normalnim nalazima, stvara ne samo zabunu pri interpretaciji, već se često pripisuje organskim promenama u bulbusu koje de facto ne postoje.

Poučeni vlastitim iskustvom sa rendgenološkim nalazima koji se viđaju kod intermitentne invaginacije genu superior duodeni u bulbus, želeli smo da prikazom sopstvene kazuistike skrenemo pažnju na ovaj rendgenološki fenomen koga smo nazvali duodenalni genobulbarni prolaps / Prolapuss genobulbaris duodeni intermittens /.

**Materijal i metode** – Dugogodišnja plodna saradnja rendgenološke i gastroenterološke službe Univerzitetskog kliničkog centra u Beogradu omogućava potpunu i pravilnu dijagnostiku oboljenja digestivne cevi. Prema uhodanom stavu obe službe, svi bolesnici sa bilo kojim pozitivnim, sumnjivim ili nejasnim rendgenološkim nalazima upućuju se na endoskopski pregled tokom koga se uzima biopsijski materijal i gastroduodenalni aspirat. Zbog toga svaki bolesnik uz rendgenološki nalaz ima izveštaj sa gastroduodenoskopije i rezultate biohemijskih, patohistoloških i mikrobioloških pregleda.

U ovu studiju uključeno je 17 ispitanika oba pola, srednje životne starosti 41 godinu (raspon godina od 23-58) u kojih je tokom 1989. godine rendgenskim pregledom gastroduodenuma nađen promenljiv izgled bulbusa sa neuobičajenom slikom polipoidnog tumora ili niše oko kojih se koncentrično ređaju nabori sluznice. Rendgenološki nalaz je bio nestalan i smenjivao se sa normalno formiranim bulbusom bez navedenih promena što je iziskivalo endoskopski pregled. Pored ezofagogastroduodenoskopije uziman je biopsijski materijal sluznice iz antruma želuca i bulbusa, a dobijeni aspirat iz želuca i duodenuma pregledan je biohemijski, patohistološki i mikrobiološki.

**Rezultati** – U populaciji od 828 pregledanih bolesnika tokom 1989. godine sa simptomatologijom oboljenja gastroduodenuma, češće u onih

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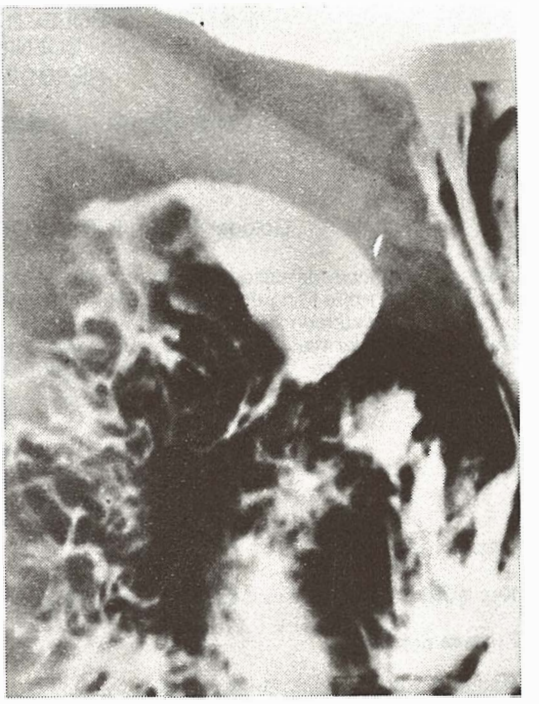
Slika 1 – Bulbus duodeni snimljen u momentu prolabiranja genu superior antiperistaltikom iz $D_2$.

Fig. 1 – The duodenal bulb imaged in the moment of superior flexure prolapsing during antiperistasis of $D_2$.



Slika 1a – Bulbus duodeni u istog bolesnika nekoliko trenutaka kasnije prikazuje tipičan nalaz pravilnog, dobro ograničenog polipoidnog tumora sa lažnom centralnom nišom ili ulkusni krater sa okolnim edemom i semicirkularnim zadebljanim naborima. Prolaps antralne sluznice daje defekt na bazi bulbusa.

Fig. 1a – The duodenal bulb in the same patient several moments later shows typical finding of an oval sharply delineated polypoid mass with a false ulcer, or an ulcer crater with surrounding edema and semicircular folds thickening. Prolapse of antral mucosa gives rise to a basal bulbar defect.

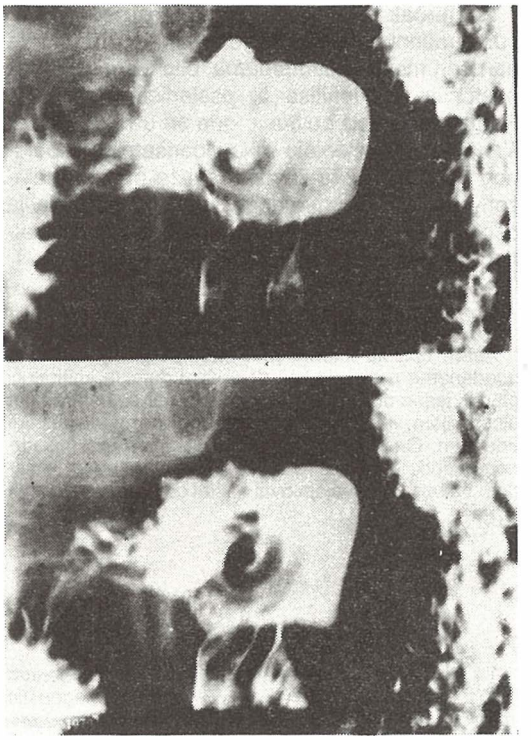
sa sumnjom na ulkusnu bolest duodenuma, u 17 (2,05%) ispitanika su nađene neuobičajene rendgenološke promene u bulbusu duodenuma. One su imitirale polipoidni tumor ili svež ulkusni krater oivičen periulkusnim edemom i grubljim polukružnim naborima koji su se ređali kao listovi lukovice (Slike 1-4).

Pažljivim radioskopskim pregledom uočeno je da takvi nalazi potiču od prolapsa gornje fleksure duodenuma u bulbus tokom antiperistatičke kretnje i mešanja kontrasta iz $D_2$ i $D_3$, a u odsustvu bilo kakve prepreke u lumenu duodenuma i proksimalnim vijugama jejunuma. Takođe je zapaženo da se u toku formiranja pseudotumora ili lažne niše u apeksu bublusa često otvara i širi pilorusni kanal kroz koji prolabira sluznica antruma u bazu bulbusa kao protuteža promeni u apeksu.

Prolaps gornjeg kolena duodenuma u bulbus je prolazna pojava i u njegovom odsustvu bulbus se pravilno oblikuje, a nabori njegove sluznice, često grubljeg izgleda poprimaju uobičajen tok.

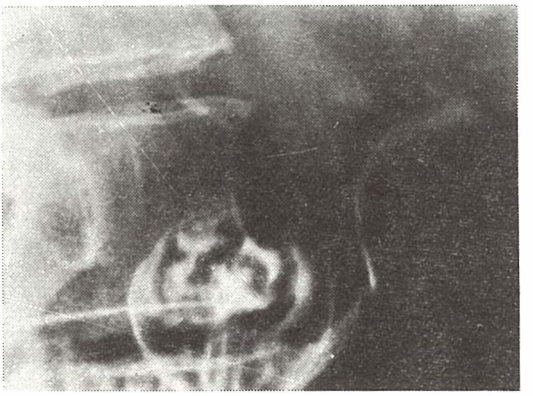
Gastroduodenoskopija u svih pregledanih sa rendgenološkim nalazom prolapsa gornje duodenalne fleksure u bulbus isključila je prisustvo polipoidnog tumora, niše ili ožiljka, mada je u većine postojao duodenitis i antrum gastritis (17-70,6%). U aspiratu antralnog i bulbarnog sadržaja u 7 bolesnika (41,1%) dokazana je Giardia intestinalis i prisustvo žučnih soli.

**Diskusija** – Povremeni rendgenološki nalaz polipoidnog defekta u apeksu bublusa najčešće sa centralnim depoom barijuma uz koncentrične nabore sluznice koji se smenjuje sa nalazom pravilno formiranog bulbusa bez defekta u kontrastnoj senci ne pripada organskoj leziji bulbusa već pseudotumoru ili lažnoj floridnoj niši zbog prolapsa gornje fleksure duodenuma u bulbus.



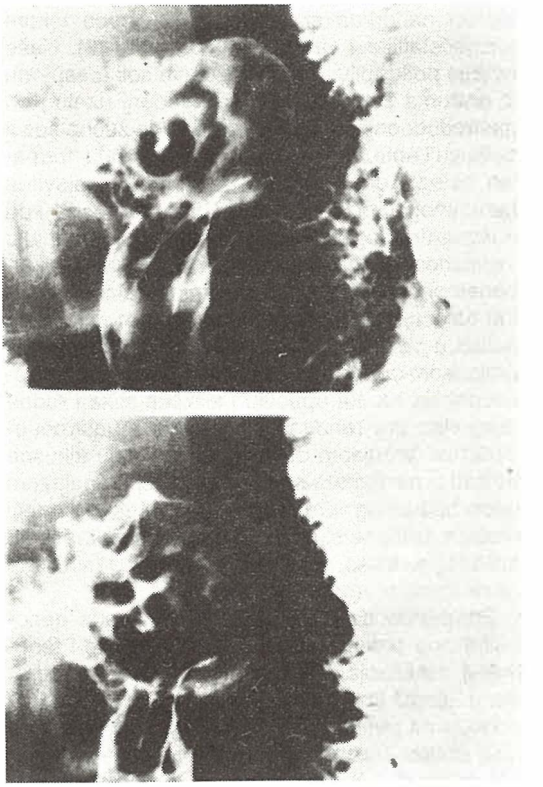
Slika 2 – Bulbarni pseudoulkus sa okolnim edemom i cirkularnim zadebljanim naborima sluznice. Nalaz odgovara prolapsu gornje duodenalne fleksure u bulbus.

Fig. 2 – Bulbar pseudoulcer with surrounding edema and circular fold thickening. The finding corresponds to a prolapsed superior duodenal flexure.



Slika 4 – Dvojno kontrastni pregled retroantralnog bulbusa prikazuje cirkularne, zadebljane nabore sluznice oko lažnog zvezdastog ulkusa.

Fig. 4 – Double contrast study of the retroantral duodenal bulb shows the circular thickened mucosal folds around a false stellate ulcer.



Slika 3 – Pravilan kružni defekt sa centralno položenom mrljom kontrasta i zadebljanim kružnim naborima sluznice u okolini. Prolaps antralne sluznice kroz pilorus je takođe vidljiv.

Fig. 3 – A round sharply delineated filling defect with central collection of barium and circular mucosal thickened folds in the surrounding. Antral mucosal prolapse through the pylorus is evident.

Tragajući u literaturi za sličnim rendgenološkim entitetom naišli smo na kratak osvrt Teplick-a i saradnika (1) koji ovaj rendgenološki fenomen nazivaju »fleksurni pseudotumor« i smatraju ga za varijantu nastalu zbog projekcije previjene gornje fleksure duodenuma preko bulbusa.

U prilog naše tvrdnje da se radi o prolapsu a ne o projekcionom fenomenu kako navodi Teplick sa saradnicima svedoče brojne činjenice. Prateći podrobno kretnje duodenuma tokom radioskopije uočili smo da antiperistatički talasi iz $D_2$ ređe iz $D_3$, utiskuju genu superior u bulbus na šta ukazuju dva uzastopna snimka u istog bolesnika (slike 1, 2). Sličan rendgenološki nalaz se viđa i opisan je kod pasaže tankog creva, kod koje se prolazna invaginacija jejunuma prepoznaje po kružnom rasvetljenju oivičenom koncen-

tričnim naborima sluznice što se sreće tokom antiperistaltike i »mešanja« kontrasta (2). Naše tvrdnje potkrepljuju i nalazi žučnih soli u aspiratu iz antruma želuca i bulbusa duodeni uzetog pri gastroduodenoskopiji. Poznato je da žučne soli u bulbusu i antrumu želuca ne predstavljaju normalan nalaz i da u njih dospevaju u slučajevima narušenog motiliteta duodenuma, odnosno kod bulbo-antralnog refluksa. Žučne soli smanjuju viskoznost sluzi, redukuju pH u mukozno-bikarbonatnoj barijeri, a deterdžentnim efektom direktno oštećuju sluznicu antruma (3). Patohistološki nalazi u većine pregledanih sa geno-bulbarnim prolapsom odnose se na antrum gastritis i gastroduodenitis na šta upućuju i klinička slika i radne dijagnoze pre rendgenskih pregleda gastroduodenuma. Verujemo da simptomatologiju ulkusne bolesti u pacijenata sa rendgenološkim nalazom geno-bulbarnog prolapsa daje i često prateći prolaps antralne sluznice transpilorično kao izraz antrum gastritisa, odnosno izmenjenog motiliteta gastroduodenuma.

Smatramo da u mehanizmu nastanka geno-bulbarnog prolapsa pored antiperistaltike i fenomena »mešanja« duodenalnog sadržaja, određenu ulogu imaju i različiti položaji $D_1$ i $D_2$ u odnosu na peritoneum. Duplikatura peritoneuma koja oblaže bulbus se upravo preko genu superior pruža naviše kao ligamentum hepatoduodenale, postavljajući gornju fleksuru i niže delove duodenuma retroperitonealno. Antiperistaltika iz manje pokretnog $D_2$ utiskuje genu superior u pokretni $D_1$, a tome pogoduju zapaljenjska stanja u duodenumu (Giardia intestinalis) u kojima je zbog povećane iritabilnosti sluznice izmenjen i motilitet zidova duodenuma.

**Zaključak** – Intermitentni prolaps genu superior duodeni u bulbus je rendgenološki izraz za narušen motilitet duodenuma, bilo da je on uzrok nastanka duodenitisa ili posledica te pojave. Promenjiv izgled bulbusa, gde se u rendgenološkom nalazu smenjuje slika ulcerisanog polipoidnog pseudotumora ili lažne sveže niše sa nalazom pravilno formiranog bulbusa, predstavlja osnovu za rendgenološku dijagnozu duodenalnog geno-bulbarnog prolapsa.

**Sažetak**

Autori opisuju intermitentni prolaps gornje fleksure duodenuma u bulbus koji daje sliku defekta imitirajući gladak jasno ograničen polipoidni tumor sa centralnom ulceracijom ili svež ulkusni krater sa periulkusnim edemom. Grubi cirkularni nabori sluznice oko fleksurnog pseudotumora ili lažne niše sa promenjivim izgledom bulbusa razdvajaju ovaj entitet od pravih bulbusnih lezija.

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CLINICAL HOSPITAL DR M. STOJANOVIĆ, ZAGREB
DEPARTMENT OF RADIOLOGY AND ONCOLOGY

# A CASE OF ISCHAEMIC ENTERITIS

Zamberlin R, Bedek D, Smolčić S

**Abstract** – The article describes ischaemic disease of the small intestine. A case is examined from the pathological and clinical points of view, with special emphasis on the radiological aspect. In the etiology of this disorder, the meaning of the so–called »low flow state« has been emphasized which is a more frequent cause of ischaemia of the bowel than is occlusive disease of the blood vessels.
The radiological symptomatology on plain films of the abdomen is often rather poor and nonspecific. Therefore, angiography is very seldom performed, but nevertheless may have diagnostic and therapeutic value. A barium enema examination of the small intestine reveals thickened folds and peripheral filling defects, thumbprint indentations, deformities of the wall due to submucosal edema and hemorrgahes. It is possible to see ulcerations and later narrowing of the affected intestinal loops as in Crohn's disease. The case study is of a 76–year–old female. The results of our study were verified by a barium enema examination of the small intestine and autopsy.

**UDC:** 616.34-005.4

**Key words:** enteritis-radiography, ischemia

**Case report**

**Radiol Iugosl** 1991; 25:15– 7.

**Introduction** – In general hospitals, acute ischaemic disease of the small intestine occurs in one in a thousand hospitalized patients (1). Occlusive disorders of the blood vessels of the small intestine, which in the last stage of their evolution lead to fatal mesenteric thrombosis, are the cause of ischaemic diseases of the intestine in approximately half of the cases. The second and probably larger group of vascular disorders of the intestine are not of an occlusive nature, but occur as so–called »low flow states« such as hypotension, shock, cardiac decompensation as well as with the use of digitalis preparations and certain vasopressors (2,3). Thromboembolic complications are increasingly mentioned in conjunction with oral contraceptives. Small blood vessel damage in cholagenosis, diabetes mellitus as well as radiation damage are predisposing factors in the development of this disease.

The pathological occurrences in ischaemic intestinal disorders are manifested by various symptoms and signs, depending on the etiology and the activity of pathogenic bacterial flora. In reduced mesenteric circulation, there are severe and long–lasting splanchnic vasoconstriction, a reduction in biosynthesis, nausea, the epithelial cells become sensitive to trypsin intestinal juice, and pancreatic endopeptides digest the subepithelial structures. Submucosal edema occurs as well as hemorrhage and necrotization of inflamations in the affected intestinal segment (1,4). The clinical manifestations of ischaemic enteritis often precede the pathological condition accompanying hypotension (myocardial infarction, severe trauma, surgery). The disease begins suddenly with spasmodic pain in the abdomen with the frequent presence of vomiting and diarrhoea. The stool is mucilaginous and blood–stained (5). Ischaemic enteritis should be clinically suspected in every patient with acute initial undefined abdominal pain and bleeding from the gastrointestinal tract.

A plain film of the abdomen in ischaemic enteritis can show dilated coils of the small intestine with the fluid level, eventual wavey contours and shifting of the coils due to wall thickening, but the more frequent finding is entirely nonspecific. The presence of air in the intestinal walls suggests gangrene, and air in the portal vein is a sign of the nearly fatal result of the disease.

In barium enema, the most significant finding is a wavey contour like a thumbprint and separa-

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tion of the coils, narrowing of the lumen and occasional ulceration of the mucosa. In suspected ischaemia, angiography would be the method of choice because it can be both diagnostic and therapeutic, but today it is rarely performed (6).

**Materials and methods** – We present a case of ischaemic enteritis in a 76-year-old female patient. The course of the disease lasted 24 days, during which several plain radiograms of the abdomen were performed, as well as abdominal CT, irrigography, and on the fourteenth day a barium enema of the small intestine by which ischaemic ileitis was confirmed.

The patient had been a type–2 diabetic for many years, hypertonic, and cardiopathic with atrial fibrillation. Three years previously she had experienced a cerebrovascular insult with right-sided haemiparesis. On the twenty-fourth day of the illness, there was worsening with spasmodic pain in the abdomen, a drop in blood pressure and lethal exitus. Autopsy was performed which confirmed the finding of ischaemic enteritis.

**Results** – The patient was received at the Department of Gastroenterology of the Clinic of Internal Medicine due to sudden severe spasmotic pains in the abdomen which had begun the day earlier, of undefined localization and accompanied by vomiting and diarrhea (five grey mealy stools mixed with red mucosal admixture). Immediately prior to her arrival in hospital, the patient expelled vomitus of dark content with remains of food. Plain X-ray of the abdomen upon arrival showed no signs of ileus. On the fourth day of illness, the abdominal X-ray showed distension of the coils of the jejunum with marked thickening of the Kerkring folds with an aeroliquid level in the intestines. On the twelfth day, there were no signs of ileus on the plain abdominal X-ray. Irrigographic findings were normal. On the fourteenth day, the barium enema examination of the small intestine revealed regular macrorelief of the jejunum whereas in the area of the ileac coil in the second segment relateve stenosis was visible with a loss of elasticity (Figure 1). Multiple ribbed defects like thumbprints are visible with smaller deposits of contrast medium which correspond to submucosal necrosis and minor ulceration (Figure 2). The terminal ileum was intact. On autopsy, a long ischaemic segment of the ileum was found without visible mesenteric occlusion, and histological preparation showed evidence of necroticized inflammation.

**Discussion** – The radiologic symptomatology of ischaemic enteritis on plain film of the abdo-

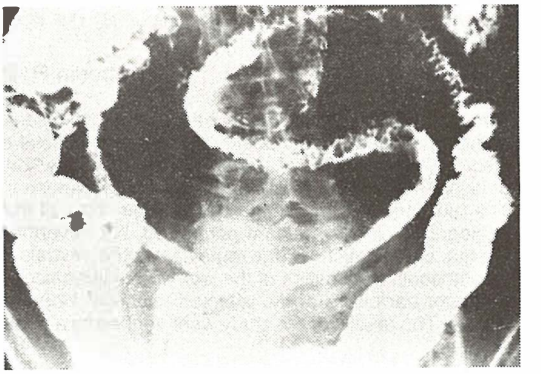

Fig. 1. – Barium small bowel examination shows distorted macrorelief and inactive segment of the bowel.

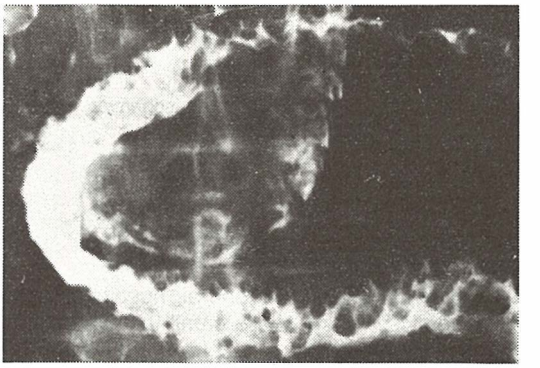

Fig. 2 – »Thumb-printed« deformities in the wall of the small bowel caused by ulcerations and mucosal and submucosal haemorrhages.

men is often meager and nonspecific (aeroliquid level, distension of coils of the small intestine, thickening of intestinal walls). Angiography is rarely performed due to the generally poor condition of the patient or due to clinically insufficiently clear pictures.

The radiological image of ischaemic enteritis in the barium enema examination of the small intestine can be identical with Crohn's disease. Nevertheless, the characteristic »skip« lesion and short affected segments of the intestine in Crohn's disease differ from ischaemic enteritis. In differential diagnosis, we mention carcinosis of the peritoneum which can yield a radiologic picture similar to that of ischaemic changes.

**Conclusion** – The purpose of this presentation is to call attention to clinical, radiological and patho-anatomical entity of ischaemic enteritis with the observation that this disease should be

clinically suspect in each patient with acute initial nondefined abdominal pain accompanied by bleeding from the digestive tract. The relatively infrequent cases of ischaemic disease of the small intestine, which are clinicaly recognized, radiologically investigated and eventually verified by autopsy is a sign of the inadequate active approach to such patients, primarily by the clinician, but also by the radiologist.

**Sažetak**

SLUČAJ ISHEMIJSKOG ENTERITISA

Opisana je ishemijska bolest tankog crijeva s patologijskog i kliničkog aspekta s posebnim osvrtom na radiologijsku sliku.

U etiologiji bolesti ističe se važnost tzv. stanja usporene cirkulacije krvi – »low flow state« – koje je općenito češći uzrok ishemije tankog crijeva nego okluzijske bolesti krvnih žila. Radiologijska simptomatologija na nativnim rendgenogramima abdomena često je oskudna i nespecifična, angiografije se rijetko izvode, ali mogu uz dijagnostičku imati i terapijsku vrijednost. Kod pasaže tankog crijeva ishemijski se enteritis manifestira zadebljanjem nabora i rubnim defektima punjenja – »otisci prsta« – zbog submukoznog edema i hemoragije. Mogu se vidjeti ulceracije, a kasnije i suženje lumena jednog segmenta tankog crijeva, što posve nalikuje Crohnovoj bolesti.

Prikazujemo naš slučaj ishemijskog enteritisa u 76 godišnje pacijentice utvrđen pasažom tankog crijeva i verificiran obdukcijskim nalazom.

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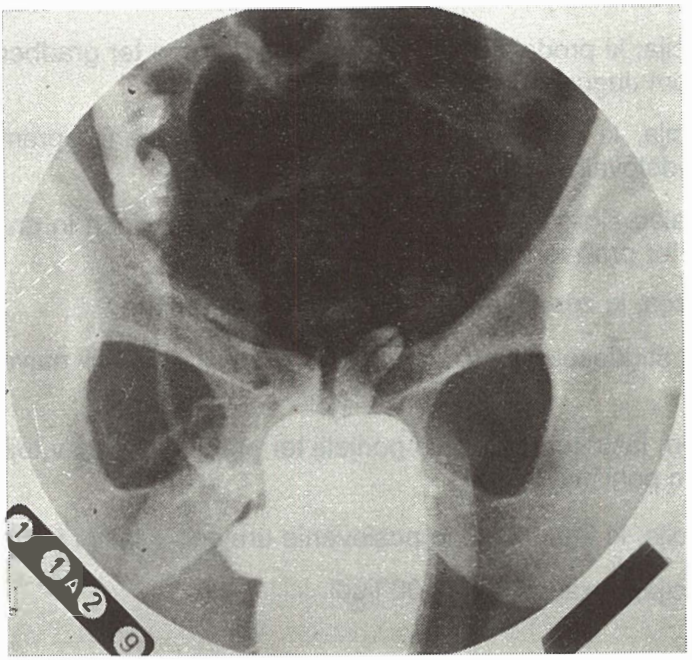


Figure 1

(For answers see page 61!)

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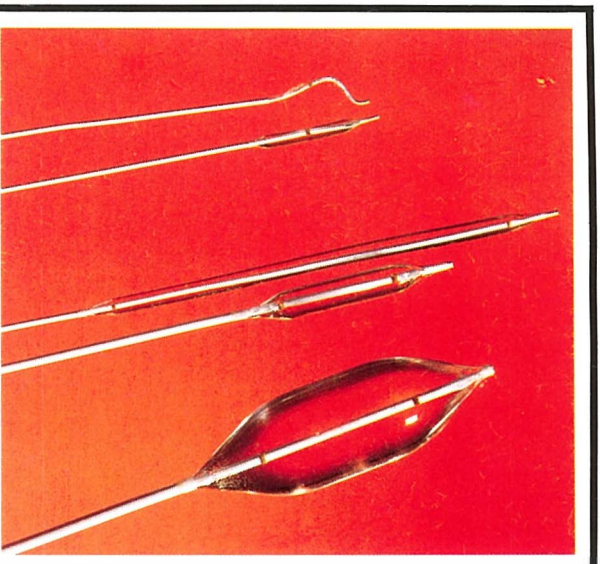

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ZAVOD ZA RADIOLOGIJU I ONKOLOGIJU

# ANGIOGRAFSKA I CT DIJAGNOSTIKA TROMBOZE GORNJEG SAGITALNOG SINUSA

## ANGIOGRAPHY AND CT IN THE DIAGNOSIS OF SUPERIOR SAGITTAL SINUS THROMBOSIS

Klanfar Z, Hat J

**Abstract** – The authors have presented angiographic and CT changes in patients with thrombosis of the superior sagittal sinus and cortical ascending veins of the brain. The etiology and clinical picture of pathological processes as well as the complied experience related to angiography and CT diagnostics are described. The relevance of differential diagnosis and the sources of diagnostic errors are pointed out.

**UDC:** 616.145.11-005.6-073.75

**Key words:** dura mater, sinus thrombosis, angioplasty, tomography x-ray computed

**Profess paper**

**Radiol Iugosl** 1991;25:21-5.

**Uvod** – Tromboza moždanih vena i sinusa je teško kliničko stanje koje prijeti ozbiljnim komplikacijama ukoliko izostane pravovremena dijagnoza i svrsishodna terapija. Tromboze je moguće razvrstati u septičke i aseptičke a njihova učestalost je veća nego se prema broju publiciranih slučajeva pretpostavlja. Uzroci septičkih tromboza su lokalne ili udaljene infekcije dok aseptičke tromboze imaju brojne predispozicijske i uzročne faktore; oralna kontracepcijska sredstva, trudnoća i puerperij, trauma lubanje, kraniotomija, subarahnoidalno krvarenje, vaskularne malformacije, srčane bolesti s venskom kongestijom, dehidratacija organizma i hiperkoagulabilna stanja.

Početni simptomi i klinički znaci bolesti mogu biti nespecifični i raznoliki. Najčešći su glavobolja, povraćanje, edem papile, promjene svijesti i koma. Uzrokovani su povišenim intrakranijskim pritiskom a kliničkim metodama teško ih je uzročno povezati. U svom daljnjem toku bolest se komplicira intracerebralnim i subarahnoidalnim krvarenjem te infarktima u zoni tromboze moždanih vena, što uzrokuje konvulzije i pojavu pareza. Gornji sagitalni sinus (GSS) može biti djelomično ili potpuno okludiran trombom a tromboza se najčešće širi i u kortikalne ascendentne vene koje se ulijevaju u njega (1–8).

U dijagnostici tromboze GSS koristimo cerebralnu angiografiju, kompjuteriziranu tomografiju mozga (CT) i pretragu mozga magnetskom rezonancom (MR). Prikazom promjena u angiogramima i CT presjecima vlastitog bolesnika želimo doprinjeti boljem poznavanju dijagnostičkih mogućnosti za rano otkrivanje tromboze GSS.

**Materijal i metoda** – Bolesnik K. J, 37 god. imao je 10 dana mučninu i frontalne glavobolje i povremeno je povraćao. Kod prijema u bolnicu krvni pritisak mu je bio normalan, cerebrospinalni likvor je bio krvav a CT pretragom smo dokazali krv u subarahnoidalnim šupljinama mozga.

Pošto cerebralnom panangiografijom nismo dokazali uzrok krvarenja bolesnik je otpušten kući. Nakon 2 mjeseca on je ponovno primljen u bolnicu zbog kontrolne CT i angiografske pretrage. Kod prijema bolesnik je u dobrom općem stanju i bez neuroloških tegoba. Niti ponovljenom cerebralnom angiografijom nismo dokazali uzrok ranijeg krvarenja ali su na angiogramima bili prisutni znaci tromboze GSS i terminalnih dijelova ascendentnih kortikalnih vena. CT pretraga je potvrdila ovaj nalaz.

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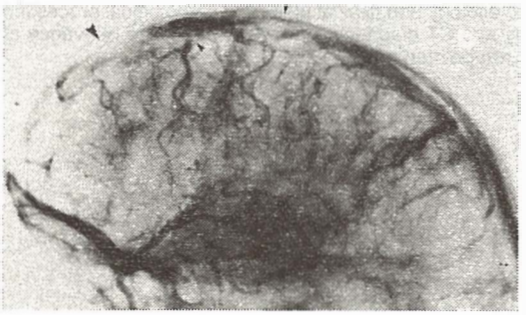
Kod angiografije smo selektivno kateterizirali obje unutarnje karotidne arterije (ACI) i vertebralnu arteriju (AV). Koristili smo nejonsko niskoosmolarno kontrastno sredstvo (KS) joheksol (»OMNIPAQUE« 300) i snimali u seriji. Kod CT pretrage snimali smo nativno i nakon infuzije 250 ml 66% vodenog rastvora jonskog KS megluminioksitalamata (»TELEBRIX« 45). Snimali smo u transverzalnim i izravnim frontalnim presjecima debljine 2 i 4 mm.



Slika 1 – Profilni angiogram venske faze arteriografije desne ACI pokazuju trombozu GSS (velike strelice) i ascendentalnih kortikalnih vena (mala strelica)

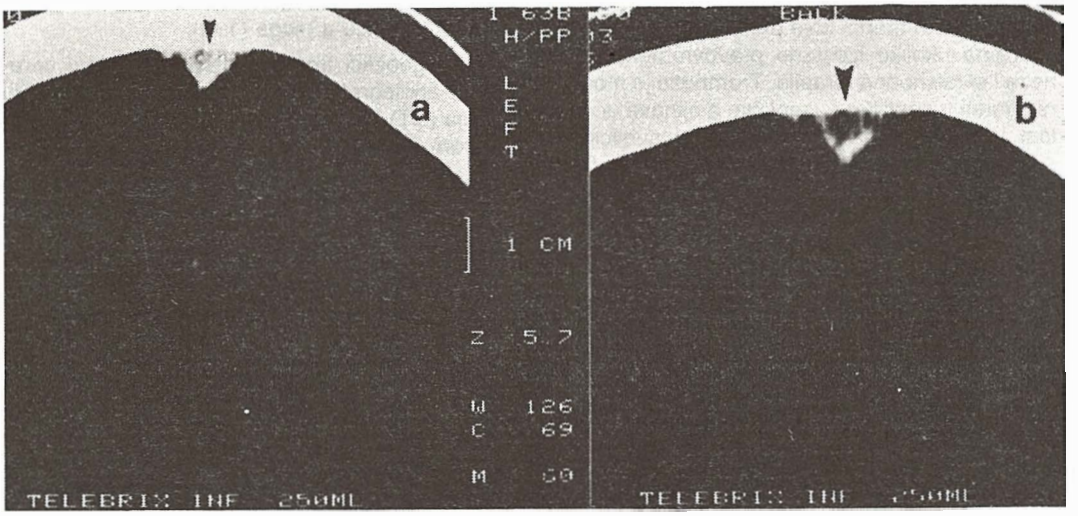
Fig. 1 – Profile angiogram of the venal phase of right ACI arteriography imaging thrombosis of the superior sagittal sinus (big arrows) and ascending cortical veins (small arrow)

**Rezultat** – U angiogramima arterijske faze cerebralne panangiografije nisu bile vidljive patološke promjene. Angiogrami venske faze pokazali su djelomično punjenje GSS te obliteraciju terminalnih dijelova većeg broja kortikalnih ascendentnih vena obih moždanih hemisfera. Vrijeme cirkulacije je bilo produženo a venski protok odvijao se pretežno dubokim venskim sustavom i preko vena fose Silvii (slika 1).

U nativnim CT presjecima nisu bile vidljive patološke promjene. Nakon infuzije KS prikazali smo na frontalnim presjecima defekt punjenja u GSS, apsorpcijskih vrijednosti 55–60 HU (slika 2a, 2b).

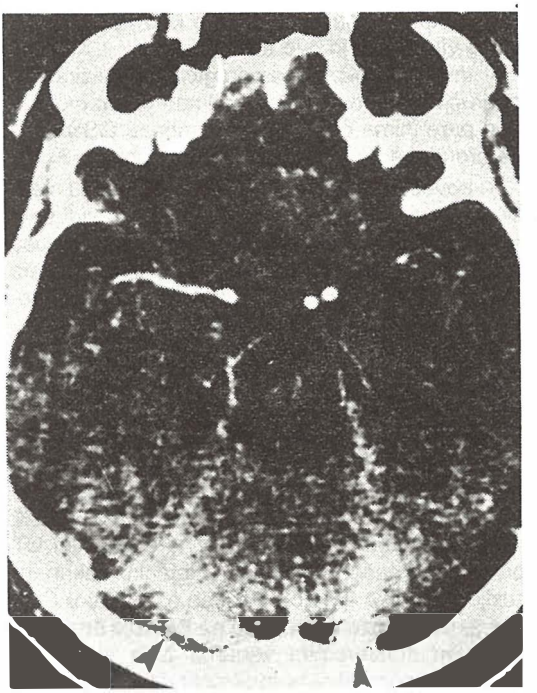
Na transverzalnim slojevima, nakon injiciranja KS, vidljivo je izrazito bojenje tentorija (slika 3) ali se prikazala i linearna hiperdenzna struktura u području inzule desne moždane hemisfere (slika 4).

**Diskusija** – U angiogramima bolesnika s trombozom GSS obično se vidi izostalo ili samo djelomično punjenje njegovog lumena. Kortikalne



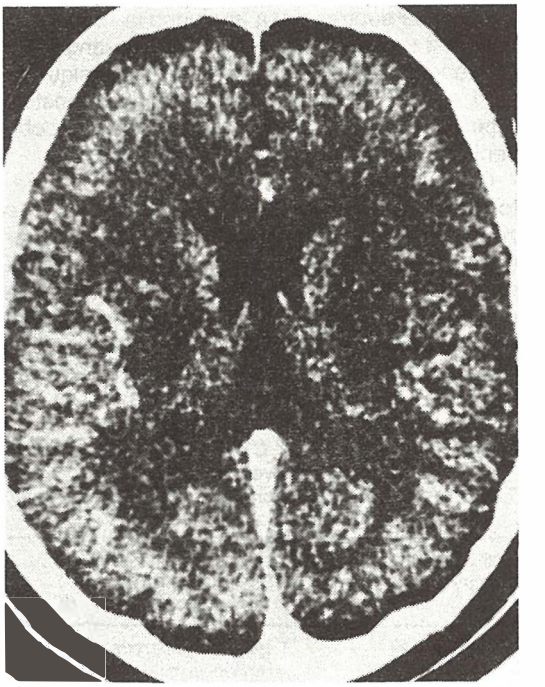

Slika 2 – a: Izravni frontalni CT presjek nakon infuzije KS kroz prednji dio GSS pokazuje defekt punjenja u lumenu (mala strelica), apsorpcijskih vrijednosti 60 HU. b: Detalj frontalnog presjeka kroz srednji dio GSS. Tromb u lumenu sinusa označen velikom strelicom

Fig. 2 – a: Filling defect in the lumen (small arrow) of 60 HU absorption value evident on direct frontal CT scan after contrast medium infusion through the frontpart of the superior sagittal sinus. b: A detail of frontal CT scan of the middle part of the superior sagittal sinus. Thrombus in the lumen is marked by a big arrow.



Slika 3 – Transverzalni CT presjek nakon infuzije KS pokazuje intenzivno bojenje tentorijuma (velike strelice)

Fig. 3 – Transverse CT scan after infusion of contrast medium images marked tentorial uptake (big arrows) arrows)



Slika 4 – Transferzalni CT presjek nakon infuzije KS pokazuje hiperdenznu linearnu strukturu u desnoj inzuli (proširena vena)

Fig. 4 – Transverse CT scan after infusion of contrast medium shows a linear hyperdense structure in the right insula (varicose vein)

vene mogu također u većoj ili manjoj mjeri biti trombozirane. Ovakve promjene vidljive su i u angiogramima našeg bolesnika. Kolateralni se krvotok odvija preko diploičnih i subgalealnih vena, ekstraduralnih venskih puteva (sinus sfenoparietalis), transduralnih vena, anastomotske Trolardove i gornje oftalmičke vene. Gornja oftalmička vena često se prikazuje kod tromboze srednje i stražnje trećine GSS a rijetko kod tromboze njegovog prednjeg dijela. Važno je znati da se ova vena ponekad vidi i kod normalnih angiografija mozga ili u slučaju povišenja intrakranijskog pritiska druge etiologije (tumor) (4,5). Izostanak prikaza prednje trećine GSS nije siguran znak njegove tromboze budući da je on hipoplastičan ili aplastičan u ovom dijelu kod izvjesnog broja ljudi. Ovakav nalaz češći je kod djece (5,6).

U slučaju sumnje na trombozu GSS korisno je provesti određene modifikacije kod cerebralne angiografije. Upotrebom dva katetera i istovremenim injiciranjem KS u obje ACI postiže se bolji prikaz GSS jer izostaje razrjeđenje neobojenom krvlju iz suprotne moždane hemisfere. Komprimiranje jedne zajedničke karotidne arterije kod standardne arteriografije ACI suprotne strane ima istu svrhu. Snimati treba u tipičnoj profilnoj projekciji i u modificiranoj okcipitalnoj projekciji glave jer će se GSS bolje prikazati ako mediosagitalnu ravninu glave nagnemo za $10^{o}$ na jednu stranu (4).

Kako bi izbjegli pogrešnu dijagnozu (lažno pozitivnu dijagnozu tromboze moždanih vena i sinusa) pri očitavanju nalaza u angiogramima treba misliti na nekoliko faktora. Pogreška je moguća zbog (4,7):

a) pseudodefekta u lumenu sinusa koji je uzrokovan utokom neobojene krvi iz drugog opskrbnog područja.

b) izostalog prikaza normalne, prohodne vene kojom struji neobojena krv kao posljedica okluzije na drugom mjestu.

c) normalnih varijacija vena i venskih anastomoza.

d) tehnički loše angiografije uslijed male količine KS, malog broja angiograma venske faze i loše projekcije pri snimanju.

Digitalna suptrakcijska angiografija (DSA) ima prednost u odnosu na konvencionalnu angiografiju zbog dijagnostičke efikasnosti, veće sigurnosti i manjih troškova. Bolji se prikaz postiže arterijskom DSA premda su dobri rezultati dobiveni i nakon intravenskog injiciranja KS (9).

CT je vrijedna i pouzdana dijagnostička metoda za dokazivanje tromboze GSS. Kako se znaci tromboze u nativnim presjecima i presjecima nakon injiciranja KS razlikuju i dijagnostički nadopunjavaju, potrebno je provesti oba načina snimanja. U tabeli 1 smo prikazali promjene, poredane prema učestalosti, koje su dokazane kod većeg broja bolesnika s trombozom GSS ali i ostalih moždanih vena i sinusa (3,6):

Tabela 1 – Promjene u CT presjeku kod tromboze moždanih vena i sinusa
Table 1 – CT evidence of changes in thrombosis of the brain veins and sinuses

| Nativni presjek<br>Primary CT-scan | Presjek iza injiciranja KS<br>CT-scan after injection of contrast medium |
|---|---|
| 1. mali ventrikli<br>small ventricles | 1. pojačan giralni crtež<br>enhanced giral lines |
| 2. znak tračka<br>cord sign | 2. defekt punjenja u sinusu (GSS)<br>empty delta sign |
| 3. hemoragični infarkt<br>hemorrhagic infarction | 3. pojačano bojenje tentorija<br>enhanced tentorial uptake |
| 5. intracerebralni hematom<br>intracerebral hamatoma | |

Legenda: KS – kontrastno sredstvo, GSS – gornji sagitalni sinus
Legend: KS – contrast medium, GSS – superior sagittal sinus

– maleni ventrikli su nespecifičan znak prisutan kod trećine bolesnika analizirane grupe od 31 bolesnika. Kod 5 bolesnika s angiografski dokazanom trombozom GSS edem mozga i maleni ventrikli bili su vidljivi u akutnoj i subakutnoj fazi tromboze, dok je u kasnijem toku bolesti uslijedilo njihovo proširenje (10). Diferencijalno dijagnostički treba pomišljati na difuzni posttraumatski edem mozga, pseudotumor, intrakranijsku hipertenziju i upalna stanja (3).

– znak tračka (cord sign) drugi je po učestalosti znak koji nalazimo u nativnim CT presjecima. Prikazuje se kao linearna hiperdenzna struktura a odgovara tromboziranoj veni (3,7).

– intracerebralno krvarenje u jednoj ili u obje moždane hemisfere dokazano je u 20% bolesnika ispitivane grupe (3). Intracerebralno i subarahnoidalno krvarenje je posljedica ekstravazacije kroz nekrotičnu stijenku tromboziranog sinusa. Subarahnoidalno krvarenje kod našeg bolesnika vjerojatno je ove etiologije.

– infarkti, obično hemoragični, lokalizirani u području tromboziranih vena kao i edem moždanog parenhima često prate trombozu GSS. Ove se promjene dobro vide u CT presjecima (8).

– povećanje apsorpcijskih vrijednosti u venskom sinusu znak je prisustva tromba i vidi se u nativnim presjecima. Tromb poprima oblik sinusa te se na frontalnim presjecima vidi trokutasta hiperdenzna tvorba koja je bazom okrenuta kostima svoda lubanje, a vrškom šupljini kranijuma. U subakutnoj fazi tromb može postati izodenzan ili hipodenzan i tada se slabo prikazuje u nativnim presjecima (6).

– defekt punjenja u GSS koji je obojen s KS vidi se najbolje u izravnim frontalnim presjecima (empty delta sign). Ova je promjena vidljiva već u ranoj fazi tromboze a opisana je u 35–72% bolesnika. Dobro je prikazana na frontalnim CT presjecima našeg bolesnika učinjenim nakon infuzije KS (slika 2a, 2b). Radi se o trombu u GSS koji je hipodenzan u odnosu na KS koje se nalazi u malim kolateralnim venama zida sinusa, u granulacionom tkivu resorbiranih dijelova tromba i u krvi koja struji kroz neokludirani dio lumena GSS (6,11). U diferencijalnoj dijagnozi treba misliti na visoko račvanje GSS, epiduralni apsces i druga ekstraduralna patološka stanja u blizini GSS (3).

– pojačan giralni crtež nakon injiciranja KS, uz ishemične ili hemoragične promjene u parenhimu mozga, dokazan je u 32% bolesnika.

– intenzivno bojenje tentorija s KS rijedak je znak tromboze GSS, a pretpostavlja se da je posljedica proširenja kolateralnih venskih puteva. Češće se vidi uz trombozu sinus rektusa. Ovu promjenu smo vidjeli na transverzalnim presjecima našeg bolesnika (slika 1d).

– prikaz proširenih transcerebralnih medularnih vena u presjecima nakon injiciranja KS rijedak je ali možda patognomoničan znak tromboze vena mozga (12). Dokazali smo ga na poprečnim presjecima našeg bolesnika nakon injiciranja KS (slika 4).

Opisane promjene u CT presjecima mogu biti oskudno izražene a poznati su i slučajevi tromboze moždanih vena i sinusa kod kojih je CT nalaz bio normalan. Stoga je indicirano suspektnu dijagnozu potvrditi jednom od komplementarnih radioloških dijagnostičkih metoda (angiografija, MR) (3,7,13). Ravnina CT presjeka ima značaj u dokazivanju tromboze GSS budući da se njegov stražnji segment u transverzalnim presjecima prikazuje dobro a stražnji segment slabo.

Zbog toga je korisno provesti snimanje i u izravnim frontalnim presjecima jer rekonstruirani frontalni presjeci mogu biti dijagnostički insuficijentni.

**Sažetak**

Autori su prikazali angiografske i CT promjene kod bolesnika s trombozom gornjeg sagitalnog sinusa i kortikalnih ascendentnih vena mozga. Opisana je etiologija i klinička slika patološkog procesa kao i kumulirana iskustva vezana uz angiografsku i CT dijagnostiku. Istaknut je značaj diferencijalne dijagnoze i opisani su izvori dijagnostičke pogreške.

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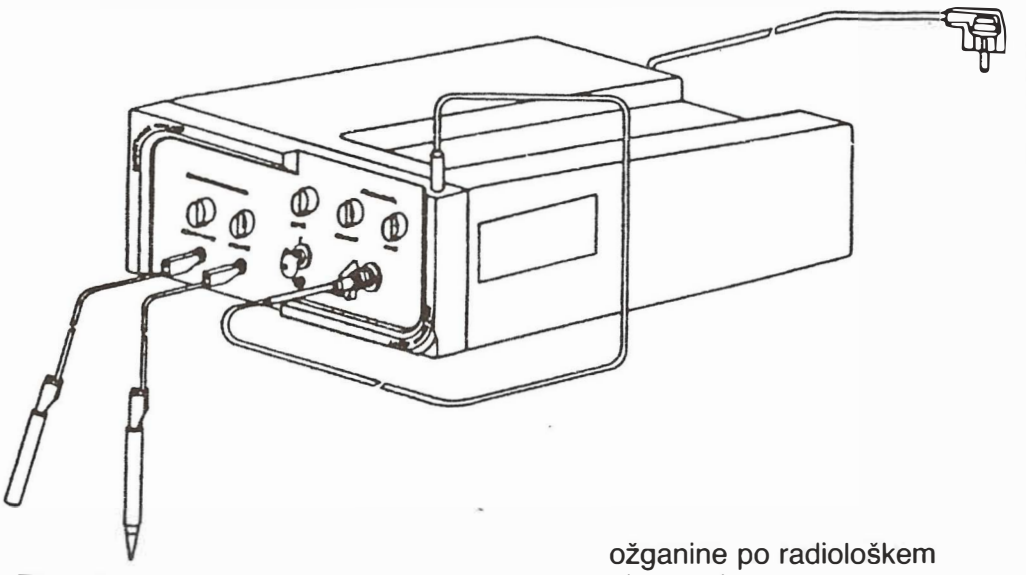

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Za osvetljevanje:
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UNIVERZITETSKO MEDICINSKI CENTAR SARAJEVO
INSTITUT ZA RADIOLOGIJU I ONKOLOGIJU

# KORELACIJA KLINIČKE SLIKE I NALAZA KOMPJUTERSKE TOMOGRAFIJE KOD KONTUZIJA MOZGA*

## CORRELATION BETWEEN CLINICAL AND COMPUTED TOMOGRAPHY FINDINGS IN BRAIN CONTUSIONS

Šlaković Š

**Abstract** – The authors have included 300 patients in the study. Out of this number, 100 patients presented the control group. Since the literature was insufficient in the explanation of the discrepancy between the injured patients with the severe clinical image and relativelly insignificant CT finding, the author payed the attention to the accurate recording and investigation of clinical parameters and postevaluation measures of the particular indexes and units, for the exact verification of the insignificant anomalies on CT scan. All measured indexes of ventricle size showed the significant difference between the group of normals and patients with diffuse edemas. The statistical analysis showed not only the significant differences between normal and pathological conditions, but also it is possible to differentiate the level of brain injuries on the basis of the mean values for the each parameter separately. The value of CT finding is expressed by the measuring of size index of interhemispheric fissures, sulcuse with and absorption coefficient. The author has proved the possibility to define exactly brain edema in the severe craniocerebral injuries and the level of these processes expansions, measuring the indexes of the quoted sizes.

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**Key words:** brain contusion, diagnosis, tomography, X-ray computed

**Orig sci paper**

**Radiol Iugosl** 1991; 25:27–34.

**Uvod** – Impozantan broj pacijenata upućenih na CT (kompjuterska tomografija) pod dijagnozom Contusio cerebri, naveo nas je da naša istraživanja prvobitno započnemo posmatranjem CT karakteristike nejasnoće u diferenciranju tipičnih kontuzionih žarišta.

Tokom četvorogodišnjeg istraživanja, zapazili smo promjene koje su našu pažnju usmjerile u drugom pravcu. Zapazili smo da određeni broj povrijeđenih sa veoma teškom kliničkom slikom u pravilu letalno završava. Na CT nisu nađene značajne promjene, posebno ne takve koje bi bile razlogom za operativni zahvat. Adekvatno objašnjenje nismo našli u literaturi.

**Materijal i metode** – Izvršili smo obradu 300 pacijenata od kojih 100 čine kontrolnu grupu. Vrednovanje CT nalaza smo vršili na osnovu sljedećih parametara: određivanje veličine komora, mjerenje koeficijenta apsorpcije moždanog tkiva na različitim mjestima, broj i širinu sulkusa na konveksitetu, određivanje širine interhemisferičnih pukotina. Iz kliničke slike izdvojili smo za korelaciju sa CT nalazima: stanje svijesti, neurološki status i izgled zjenica (tabela 1).

**Rezultati** – Na osnovu kliničkog stanja i CT nalaza formirali smo tri grupe: pacijenti sa urednim CT nalazom i stabilnim neurološkim statusom čine kontrolnu grupu a označili smo je kao grupu I. Pacijenti sa teškom kliničkom slikom i CT nalazom karakterističnim za standardne kraniocerebralne povrede (EDH – epiduralni hematom), SDH-subduralni hematom (Slika 1), ICH – intracerebralni hematom, KŽ-kontuziono žarište čine grupu II. Pacijenti svrstani u grupu III su od posebnog interesa za CT obradu. To su pacijenti sa teškom kliničkom slikom i promjenama koje odgovaraju difuznom edemu mozga a svrstali smo ih u tri podgrupe, prema izraženom procesu na osnovu CT nalaza: E1 – izraženi edem (slika 2, 3, 4, 5, 6), E2 – srednje izraženi edem (slika 7, 8) i E3 – umjereni edem (slika 9, 10). Tabela 2, tabela 3.

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Tabela 1 – Korelacija kliničke slike i CT nalaza na osnovu stanja svijesti

Table 1 – Correlation between the clinical and CT findings according to the state of consciousness

| CT nalaz<br>CT finding | Očuvane svijesti<br>Broj N° %<br>Preserved consciousness | | Poremećene svijesti<br>Broj N° %<br>Consciousness disturbances | |
|---|---|---|---|---|
| Epiduralni hematom (EDH)<br>Epidural haematoma (EDH) | 4 | 2 | 22 | 11 |
| Subduralni hematom (SDH)<br>Subdural haematoma (SDH) | 9 | 4,5 | 14 | 7 |
| Intracerebralni hematom (ICH)<br>Intracerebral haematoma (ICH) | 10 | 5 | 26 | 13 |
| Kontuziono žarište (KŽ)<br>Contusion focus | 6 | 3 | 9 | 4,5 |
| E1–izraženi edem<br>E1–pronounced edema | 2 | 1 | 76 | 38 |
| E2–srednje izraženi edem<br>E2–medium pronounced edema | 7 | 3,5 | 10 | 5 |
| E3–umjereni edem<br>E3–moderate edema | 2 | 1 | 3 | 1,5 |

Tabela 2. Parametri i indeksi kontrolne grupe po dobnim skupinama

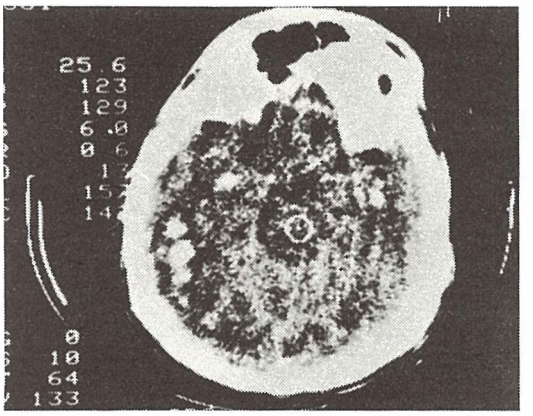
Table 2. Parameters and indexes of the control group according to age distribution

| | 0–10 | 11–20 | 21–30 | 31–40 | 41–50 | 51–60 | 61– |
|---|---|---|---|---|---|---|---|
| E u [mm] | 4,5 | 5,5 | 5,5 | 6,0 | 6,5 | 7,0 | 8,0 |
| C + D u [mm] | 42,3 | 43,2 | 43,8 | 43,8 | 44,2 | 45,1 | 47,7 |
| F/C | 1,71 | 1,80 | 1,86 | 1,90 | 1,94 | 1,98 | 2,50 |
| A/B | 4,90 | 4,70 | 4,40 | 4,50 | 4,20 | 4,00 | 3,80 |
| $0 < l < 3$ [mm] | 18 | 16 | 23 | 13 | 15 | 7 | 5 |
| $l \geq 3$ [mm] | 0 | 0 | 0 | 0 | 0 | 2 | 1 |
| $0 < S < 3$ [mm] | 18 | 16 | 23 | 13 | 15 | 8 | 4 |
| $S \geq 3$ [mm] | 0 | 0 | 0 | 0 | 0 | 1 | 2 |
| S nisu mjerljivi immeasurable | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| $B_s$ 1 do 3 | 3 | 0 | 0 | 0 | 0 | 0 | 0 |
| $B_s$ 4 do 9 | 15 | 16 | 23 | 13 | 15 | 7 | 1 |
| $B_s \geq 10$ | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Hn MS | 29,2 | 30,3 | 30,8 | 31,4 | 33,2 | 33,4 | 34,1 |
| Hn MP | 26,1 | 27,2 | 28,0 | 28,5 | 29,0 | 31,0 | 31,5 |
| Hn KM | 28,7 | 29,3 | 30,5 | 30,6 | 31,2 | 31,3 | 33,4 |

Legenda – E u mm = treći ventrikl, C + D u mm 0 Huckmann-ov indeks,
– E in mm=third ventricle, C + D in mm = Huckmann index,
– F/C = ventrikularni indeks, A/B = Cella media indeks,
F/C = ventricular index, A/B = Cella media index

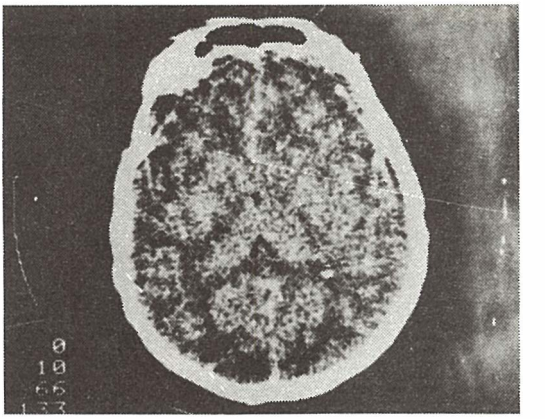
– l u mm = interhemisferične pukotine, S = širina sulkusa
l in mm = interhemisferic fissures, S = sulcus with, Bs= broj sulkusa, HnM.S = koeficijent apsorpcije u području moždanog stabla, Hn MP = koeficijent apsorpcije moždanog parenhima paraventrikularno, Hn KM = koeficijent apsorpcije na konveksitetu mozga

$B_s$ = number of sulcuses, HnMS = absorption coefficient in the zone of brain stem
HnMP = absorption coefficient of the brain parenchyma, paraventriculary
HnKM = Absorption coefficient on the brain convexity



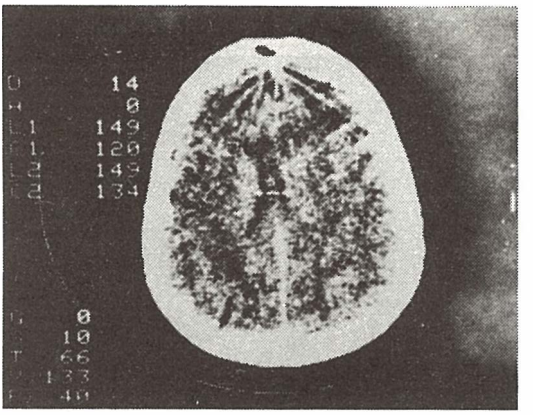
Slika 1 – Brojne hiperdenzne i hipodenzne zone tipične za kontuziono žarište

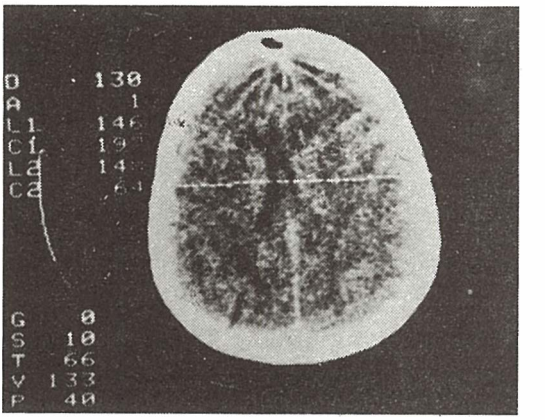
Fig. 1 – Numerous hyperdense and hypodense zones typical for the contusion focus



Slika 2 – Nevidljivi treći ventrikl kod izraženog edema (E1)

Fig. 2 – Invisible third ventricle in pronounced edema (E1)





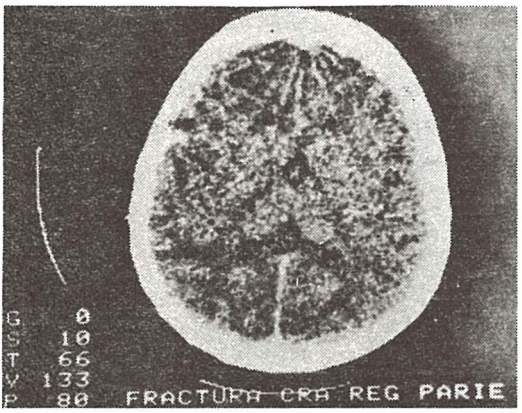
Slika 3 i 4 – Cella media index (A/B) = 9,28 karakterističan za izraženi edem (E1)

Fig. 3, 4 – Cella madia index (A/B) = 9,28 characteristic| for the pronounced edema (E1)

Komparacijom parametara i indeksa grupe I i III, uočavamo razlike u rasponima srednjih vrijednosti koje odražavaju stepen oštećenja mozga i opravdanost stepenovanja edema u tri nivoa (E1, E2, E3). Osim toga, evidentne su promjene u odnosu na grupu ispitanika sa normalnim nalazima (grupa I). Tabela 4, tabela 5, tabela 6, tabela 7.

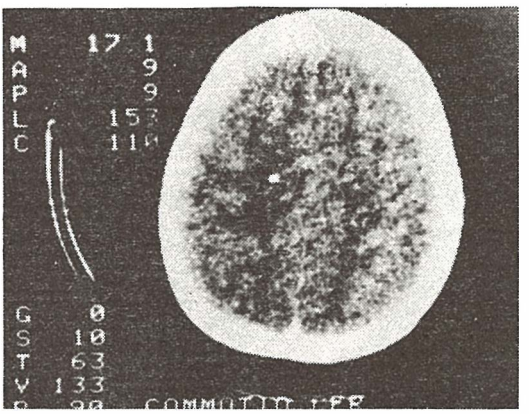
Za korelaciju kliničke slike i CT nalaza, parametar stanje svijesti je uzet u sva tri stepena. Koma, kao najizraženiji stepen poremećaja svijesti, prema našim ispitivanjima, nije karakterističan za subduralni hematom ali je izražena kod pacijenata sa kontuzionim žarištem i intracerebralnim hematomom. Duboka koma je prateći klinički simptom kod pacijenata sa E1.

Rezultat statističke evaluacije naših podataka je da ne postoji signifikantna zavisnost kliničke slike i CT nalaza u grupi II, a u grupi III postoji. U odnosu na parametar neurološki status, ne postoji signifikantna zavisnost kod grupa II i III, dok klinički znaci na osnovu pregleda očiju i zjenica nisu dovoljno evidentirani, zato statistički podaci nisu mogli biti evaluirani.



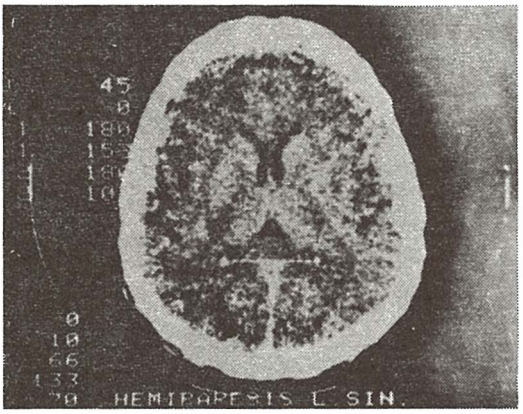

Slika 5 – Nemjerljivi ventrikli, izrazita slika difuznog edema mozga

Fig. 5 – Immeasurable ventricles, the distinc image of a diffuse brain edema



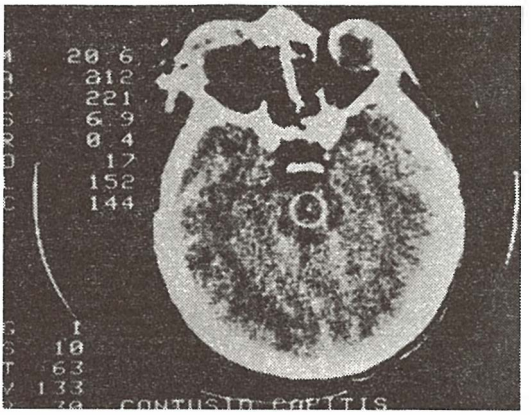

Slika 6 – Nevidljiva i nemjerljiva interhemisferična pukotina kao i sulkusi na konveksitetu mozga uz izrazito snižen koeficijent apsorpcije (17,1 Hn)

Fig. 6 – Invisible and immeasurable interhemispheric fissure and sulcuses on brain convexity with significantly decreased absorption coefficient (17,1 Hn)




Slika 7 – Ventrikularni indeks (F/C) = 1,67, koji je karakterističan za srednje izražen edem

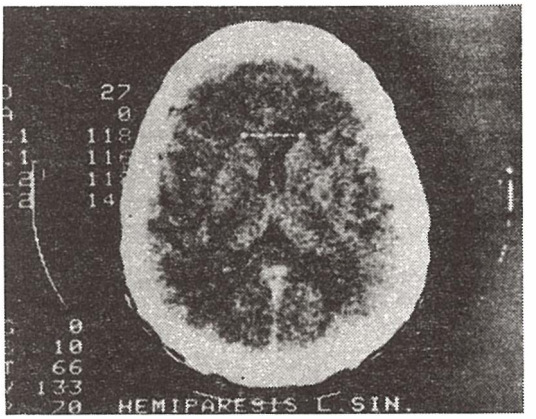
Fig. 7 – Ventricular index (F/C) = 1,67 characteristic for the meanly pronounced edema (E2)

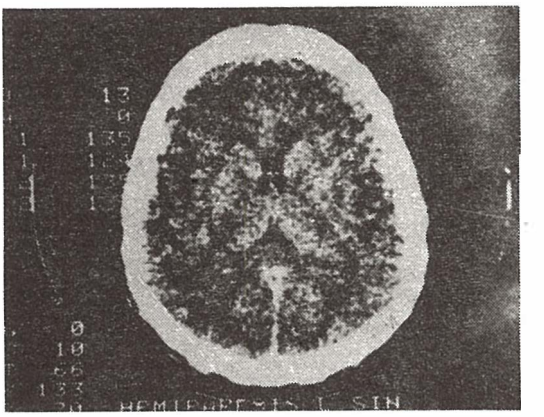



Slika 8 – Koeficijent apsorpcije (20,6 HN) na nivou moždanog stabla tipičan za srednje izražen edem (E2)

Fig. 8 – Absorption coefficient (20,6 Hn) at the level of the brain stem, typical for the meanly pronounced edema (E2)

**Diskusija –** Gyldensted (1) je izvršio mjerenje moždanog parenhima te ventrikla i sulkusa kod pacijenata oboljelih od multiple skleroze. Našao je atrofične promjene u vidu dilatacije lateralnih ventrikla i sulkusa, hipodenzne zone (paraventrikularne plakove tipične za multiplu sklerozu). Hanson et al (2) su vršili komparaciju veličina ventrikla između CT, encephalographie i echoventriculographie. Mjerili su treći ventrikl, indeks frontalnih rogova i indeks tijela postraničnih komora. Korelacija je bila oskudna. Shoek et al (3) smatra da relativno normalni CT uz teško kliničko stanje treba ponoviti jer nevidljive patološke lezije na prvom CT ne isključuju kasniju pojavu. Oni smatraju vrlo interesantnim slučajeve sa malim, nedislociranim ventriklima. Zimmerman et al (4) daju analizu CT nalaza grupe od 100 djece kod kojih uočava povećan denzitet, standardnu devi-



Slika 9 i 10 – Huckmann-ov indeks (C+D) = 40 mm, tipičan za umjereno izražen edem (E3)

Fig. 9, 10 – Huckmann index (C+D) = 40 mm, typical for the meanly pronounced edema

Tabela 3 – Srednja vrijednost parametara i indeksa I i III grupe

Table 3 – The medium value of parameters and indexes of I and III group

| | I | E3 | III E2 | E3 |
|---|---|---|---|---|
| E u [mm] | 4,5 – 8,0 | 0,0 – 0,0 | 2,0 – 4,0 | 4,0 – 5,0 |
| C + D u [mm] | 42,3 – 47,7 | 0,0 – 0,0 | 31,0 – 37,5 | 38,4 – 40,0 |
| F/C | 1,71 – 2,5 | 0,0 – 0,0 | 1,67 – 1,93 | 1,72 – 1,90 |
| A/B | 3,8 – 4,9 | 7,0 – 8,8 | 6,0 – 7,0 | 5,2 – 5,8 |
| I [mm] | $I > 0$ | nisu vidlji. invisible | $I \geq 0$ | $I \geq 0$ |
| S [mm] | $S > 0$ | nisu vidlji. invisible | nisu mjerlji. immeasurable | $S \geq 0$ |
| $B_s$ | $B_s \geq 1$ | nisu vidlji. invisible | $B_s \geq 1$ | $B_s \geq 1$ |
| Hn MS | 29,2–34,1 | 19,0–20,0 | 20,2–22,9 | 23,6–24,7 |
| Hn MP | 26,1–31,5 | 18,0–19,0 | 20,0–22,1 | 23,0–25,0 |
| Hn KM | 28,7–33,4 | 18,4–19,9 | 20,1–23,0 | 23,5–24,4 |

Tabela 4 – Korelacija kliničke slike i CT nalaza sa stepenom svijesti (grupa II)

Table 4 – Correlation of clinical and CT findings with the level of consciousness (group II)

| GRUPA II GROUP II | Svjestan Conscious | Somnolentan Somnolent | Soporozan Soporous | Komatozan Comatose |
|---|---|---|---|---|
| EDH | 4 | 11 | 1 | 10 |
| SDH | 8 | 7 | 5 | 2 |
| ICH | 10 | 12 | 3 | 11 |
| KŽ | 6 | 5 | 0 | 4 |

$X^2 = 13.9384 < 16.9332 \Rightarrow p > 0.05$

Tabela 5 – Korelacija kliničke slike i CT nalaza sa stepenom svijesti (Grupa III)

Table 5 – Correlation of clinical and CT findings with the level of consciousness (Group III)

| GRUPA III GROUP III | Svjestan Conscious | Somnolentan Somnolent | Soporozan Soporous | Komatozan Comatose |
|---|---|---|---|---|
| E1 | 2 | 14 | 9 | 53 |
| E2 | 7 | 6 | 2 | 2 |
| E3 | 2 | 0 | 1 | 2 |

$x^2 = 34.3725 > 12.7056 \rightarrow p < 0.05$

Tabela 6 – Korelacija kliničke slike i CT nalaza sa neurološkim statusom (Grupa II)

Table 6 – Correlation of clinical and CT findings with the neurologic condition (Group II)

| Grupa II<br>Group II | EDH | SDH | ICH | KŽ |
|---|---|---|---|---|
| Epilepsija<br>Epilepsy | 2 | 3 | 1 | 2 |
| Hemipareza, plegija<br>Hemiparesis, plegia | 3 | 13 | 7 | 4 |
| Disfazija, afazija<br>Disfasia, afasia | 0 | 2 | 0 | 0 |
| Horizontalni nystagmus<br>Horizontal nystagmus | 2 | 0 | 1 | 3 |

$x^2 = 11.0834 < 16.9332 \Rightarrow p > 0.05$

Tabela 7 – Korelacija kliničke slike i CT nalaza sa neurološkim statusom

Table 7 – Correlation of clinical and CT finding with neurologic status

| Grupa III<br>Group III | E1 | E2 | E3 |
|---|---|---|---|
| Epilepsija<br>Epilepsy | 0 | 1 | 0 |
| Hemipareza, plegija<br>Hemiparesis, plegia | 6 | 2 | 0 |
| Disfazija, afazija<br>Disfasia, afasia | 14 | 1 | 2 |
| Horizontalni nystagmus<br>Horizontal nystagmus | 7 | 3 | 0 |

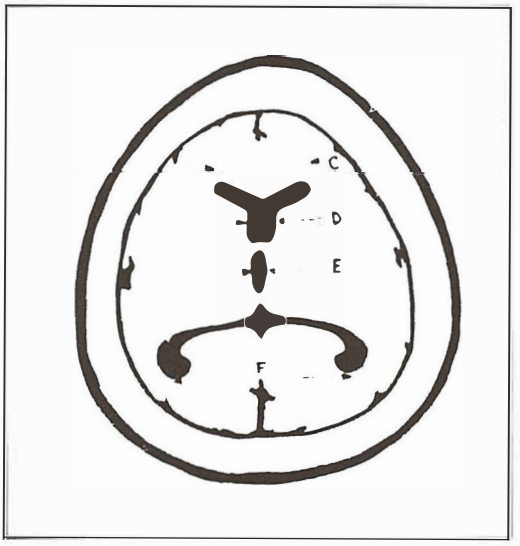
$X^2 = 8.786554 < 12.705587 \Rightarrow p > 0.05$

jaciju mjera gustine (2, 43-3, 56), male ventrikle očuvane perimenzefalične cisterne ekstracerebralne kolekcije tečnosti. Tsai et al (5) su zapazili da postoje direktni znaci traume (fokalna hemoragija, signifikantna opacifikacija parenhima kontrastnim sredstvom, hemoragična kontuzija i edem koji pokazuje različitu gustoću) i indirektni (obliteracija pontinih, cerebelontinih i perimencefaličnih cisterni). Mali četvrti ventrikl može ukazivati na edem moždanog stabla, tvrde ovi autori.

Huckmann et al (6) su vršili mjerenje ventrikla (Huckmannov broj) i četiri najuža sulkusa na konveksitetu, da bi evaluirali vrijednost CT u dijagnozi cerebralne atrofije. Grupu su sačinjavali dementni i nedementni stariji ljudi. Gawler et al (7) su vršili analizu pojedinih mjera ventrikla i sulkusa, prvo na CT a zatim na PEG-u i VEG-u kod istih pacijenata, s tim što vremenski razmak nije bio veći od 21 dan Haugh (8) saopštava da je mjerio ventrikle kod više od 170 CT skenova osoba sa normalnim neurološkim statusom.

Gyldensted et al (9) su vršili mjerenje ventrikla i sulkusa kod 100 normalnih pacijenata. Našli su da je lijevi lateralni ventrikl veći od desnog kod oba pola, te da su lateralni ventrikli veći kod muškaraca. Našli su da sa starošću rastu moždani parametri s tim što cella media indeks opada. Mjere lateralnih ventrikla pokazuju pozitivnu korelaciju s dimenzijama lubanje dok su mjere sulkusa i trećeg ventrikla neovisne od toga. Ove je parametre komparirao sa vrijednostima nađenim u literaturi na osnovu pneumoencefalografije, ultrasonografije i ventrikularnih presjeka na preparatima. Mjere ventrikla su vršili na RTG filmu ili polaroidu a ne na evaluskopu, što je iziskivalo da sve ove mjere množi sa koeficijentom uvećanja što iznosi 3, 2.

Mi smo vršili detaljna mjerenja na evaluskopu vanjskog i unutarnjeg (zida) likvorskog prostora kod 100 ispitanika sa urednim CT nalazom i stabilnim neurološkim statusom (grupa I) te na 100 pacijenata sa teškom kliničkom slikom i difuznim edemom mozga (grupa III) dijagnosticiranim na CT (shema 1)




Shema 1 – Parametri za određivanje komora

Scheme 1 – Parameter for definiton of the chamber size

E = treći ventriculus, C + D = Huckmannov index,
F/C = ventrikularni indeks
E = Third ventricle, C + D = Huckmann index
F/C = Ventricular index

Rezultati mjerenja pomoću različitih parametara za vrednovanje i obrađeni savremenim statističkim metodama ukazuje na signifikantne razlike između naših grupa i podgrupa i u rasponima srednjih vrijednosti između I i III grupe. Ovakvim mjerenjem dokazano je da se egzaktnije može odrediti postojanje difuznog edema mozga kod teških kraniocerebralnih povreda te stepen izraženosti ovog procesa a samim tim i opravdanost stepenovanja edema u tri nivoa. Osim toga, evidentne su promjene u odnosu na grupu ispitanika sa normalnim nalazima.

**Zaključak** – Mi smo utvrdili korelaciju neurološkog deficita i CT nalaza između ostalog i zbog toga što su pacijenti dopremani na CT, zbog hitnosti, bez prethodno načinjenog neurološkog pregleda. Postoji vjerovatnoća da se određeni neurološki znaci nisu imali kada razviti jer se CT pregled uradio odmah nakon povrede. Stanje svijesti, kao najpouzdaniji parametar je bio uvijek evidentiran u kliničkom statusu. Postoji korelacija poremećaja svijesti sa nalazima kompjuterizirane tomografije a posebno za teži oblik difuznog edema mozga.

Utvrdili smo normalne vrijednosti mjerljivih anatomskih struktura mozga koje su nam služile za komparaciju sa patološkim nalazima. Utvrdili smo da CT analizom možemo egzaktno dokazati prisustvo difuznog edema mozga i time kliničaru pomoći u primjeni odgovarajuće terapije. Utvrdili smo da postoje signifikantne razlike između srednjih vrijednosti parametara i indeksa za procjenu odnosa između kontrolne grupe i grupe sa difuznim edemom mozga. Takođe smo utvrdili signifikantne razlike između pojedinih stepena edema mozga klasificiranih kao E1, E2, E3. Možemo sa sigurnošću dati tačnu lokalizaciju, obim i vrstu povreda, čime omogućavamo efektniji operativni zahvat.

**Sažetak**

Izvršena je obrada 300 pacijenata od kojih 100 čine kontrolnu grupu. Kako autor u literaturi nije našao objašnjenje diskrepance između povrijeđenih pacijenata sa teškom kliničkom slikom i relativno neznatnim CT nalazom posvetio je posebno pažnju preciznom evidentiranju i izučavanju kako kliničkih parametara tako i postevalucionih mjerenja pojedinih indeksa i mjernih veličina, koje su mu onda mogle poslužiti za verifikaciju neznatne abnormalnosti na slici CT. Svi izmjereni indeksi veličina ventrikla pokazali su signifikantne razlike između grupe zdravih ispitanika i pacijenata sa difuznim edemom. Statističkom analizom, autor je pokazao da postoje ne samo signifikantne razlike između normalnih i patoloških stanja već je moguće izdiferencirati i stepen oštećenja mozga na osnovu srednjih vrijednosti svakog parametra posebno. Mjerenje indeksa veličina interhemisferičnih pukotina, širine sulkusa i koeficijenta apsorpcije sa već opisanim indeksom veličine ventrikla izražava vrijednost CT nalaza. Autor dokazuje postojanje signifikantne razlike između svih navedenih grupa i podgrupa. Time je čvršće dokazano da ovakvim mjerenjem indeksa navedenih veličina se može egzaktno odrediti postojanje difuznog edema mozga kod teških kraniocerebralnih povreda, te stepena izraženosti ovog procesa.

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# SPECT IN DIAGNOSIS OF LEGG–CALVE–PERTHES DISEASE (COMPARISON WITH PLANAR AND PIN–HOLE SCINTIGRAPHY)

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**Abstract** – In diagnosis of Legg-Calve–Perthes (LPC) disease clinical examination, X-ray, scintigraphic methods and recently NMR are used.
The pinhole scintigraphy and NMR are found the most sensitive in detection of adult aseptic femoral head necrosis. Our intention was to estimate the sensitivity of SPECT in comparison with planar and pin-hole hip joint scintigraphy. We examined 35 patients using planar and pin-hole scintigraphy, and SPECT. The patients were distributed into 2 groups: those who had only positive clinical signs of LCP disease and those who had both clinical signs and positive X-ray findings. Our results showed that SPECT is the most sensitive among scintigraphic methods (100%). Pin-hole scintigram was also highly sensitive (91%), whereas planar scintigraphy remained the least sensitive.
In our opinion it is reasonable to perform pin-hole scintigraphy when LCP disease is suspected. In the case of negative result, it is useful to perform SPECT which is the most sensitive scintigraphic method for the detection od LCP disease. It allows not only photon deficient area detection, but also a better insight into growth plates which is very important for therapy and prognosis of the disease.
Although our group of patients was rather small we consider that high sensitivity of SPECT we reached in our study might be near to NMR sensitivity.

**UDC:** 616.718.41-002.775:539.163

**Key words:** Legg-Perthes disease-radionuclide imaging

**Orig sci paper**

**Radiol Iugosl** 1991; 25:35–8.

**Introduction** – Legg-Calve-Perthes (LCP) disease (osteochondritis) is avascular necrosis of femoral growing epiphysis. The etiology is unknown, but many authors (1, 2) believe it follows the temporary interruption of vascular supply, mostly seen in the first decade of life. It rarely occurs before the age of 3 and boys are more commonly affected.

Sometimes, the only symptom is a slight pain in the medial side of the knee. In the early stages of the disease the abduction and external rotation are reduced. The disease goes through three stages: the aseptic necrosis stage, the revascularisation stage, and the stage of reossification. In the diagnosis of LCP disease, clinical examination, X-ray, scintigraphic methods (3, 4) and recently NMR are used.

Many authors have compared the sensitivity of both planar and pinhole scintigraphy, CT and NMR (5), in the detection of adult aseptic femoral head necrosis. They find the pinhole scintigraphy (6, 7) and NMR more sensitive than other methods.

Since SPECT is used in the diagnosis of avascular necrosis our intention was to estimate the sensitivity of this method in LCP disease in comparison with planar and pinhole hip joint scintigraphy.

**Material and methods** – In our investigation we examined a group of 35 patients in the age of 4 to 12. Twenty-six of them had clinical signs typical of LCP disease. In four cases the clinical signs were bilateral, while in 22 only hip joint was affected. On the whole, 30 hip joints were affected in this group. Their X-ray findings were negative.

Nine patients had both clinical signs and positive X-ray findings. In six cases changes were present in one joint, whereas in the ramaining three both hip joints were affected. On the whole, 12 hip joints were affected in this group.

All the patients were clinically examined. The X-ray and scintigraphy of hip joints were done. The scitnigraphic methods comprised planar and pin-hole scintigraphy, and SPECT.

The scintigraphy was performed 3 hours after i.v. application of 370-555 MBq $^{99}Tc^{m}$–DPD. Planar and pinhole scintigrams were obtained with a LFOV-SEARLE gamma camera, equipped with appropriate collimators. The SPECT of hip joints was obtained by means of SIEMENS–ROTA dual-head gamma camera interfaced to

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ADAC DPS-3300 computer suplied with array processor.

The parameters of acquisition are as follows: image matrix 128x128, angular sampling 6°, duration of single projection 30 sec. The entire acquisition lasts about 20 minutes. Uniformity correction is made by the help of flood source for each head of the camera (every image contains 30000 K counts and is acquired daily).

Before the reconstruction, projection images are filtered using convolution filter with cut-off frequency 0.8 Nyquist frequency. For the reconstruction of tomographic sections we used the ADAC commercial programme for backprojection and butterworth filter order 5 and cut-off frequency 0.8 Nyquist frequency.

In our opinion, the described procedure gives the most suitable images for the interpretation. The images are clear enough, smoothed and without too much noise.

**Results** – Among 26 patients with clinical signs of the disease on 30 joints, planar scintigram was positive in 14 joints, pin-hole in 21 and SPECT in 24 (Table 1). As positive we considered the scintigrams that showed photon deficient area (Fig. 1a, b, c, d, e). Six patients with clinical signs of the LCP disease had negative scintigraphic findings. The follow-up of these patients showed that they had synovitis. In the group of 9 patients with clinical signs and positive radiographic findings, three had bilateral changes and six only in one hip joint. Planar scintigram finding was positive in 8 hip joints, pin-hole in 11 and SPECT in all the 12 hip joints in this group (Table 2).

It was evident that SPECT improved sensitivity of bone scintigraphy in LCP disease (Fig. 2a, b, c).

**Discussion** – Some authors have compared the sensitivity of scintigraphy, X-ray, CT and NMR in the diagnosis of femoral head aseptic necrosis. They concluded that NMR is the most sensitive method in the diagnosis of femoral head aseptic necrosis. Recently, SPECT was introduced as a diagnostic method for femoral head aseptic necrosis. Authors have concluded that SPECT is more sensitive than planar and pin-hole scintigram (4, 8) and that the superiority of NMR as a diagnostic method is now less clear.

Table 1 – Comparison of planar scintigram, pin-hole scintigram, and SPECT in patients with clinical signs of LCP disease (n = 30)

| | Positive | Negative |
|---|---|---|
| Planar scintigram | 14 | 16 |
| Pin-hole scintigram | 22 | 8 |
| SPECT | 24 | 6 |

Table 2 – Comparison of planar scintigram, pin-hole scintigram, and SPECT in patients with clinical signs of LCP disease (n = 12)

| | Positive | Negative |
|---|---|---|
| Planar scintigram | 8 | 4 |
| Pin-hole scintigram | 11 | 1 |
| SPECT | 12 | 0 |

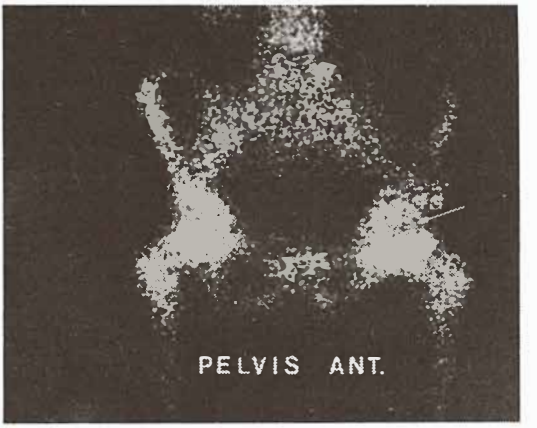



Fig. 1a – Planar scintigram of the pelvis, photon deficient area (arrow) in the left femoral head

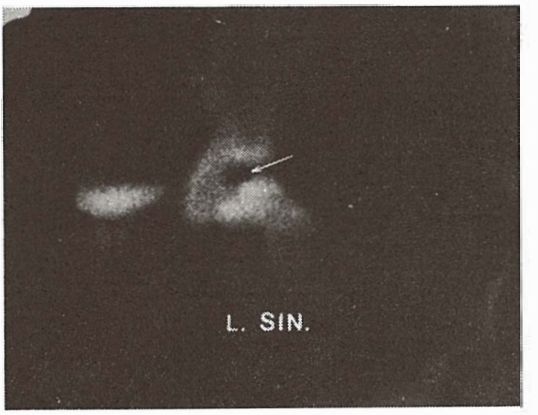
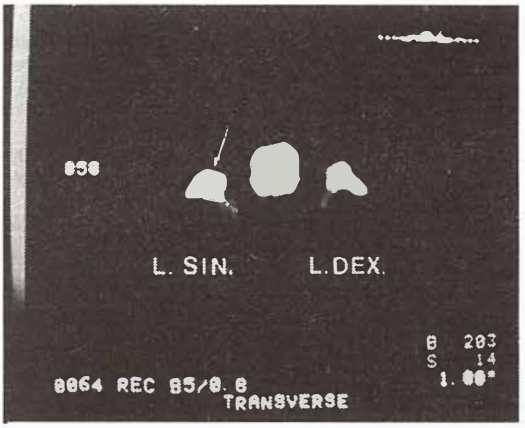



Fig. 1b – Pinhole scintigraphy of the left femoral head, photon deficient area (arrow)



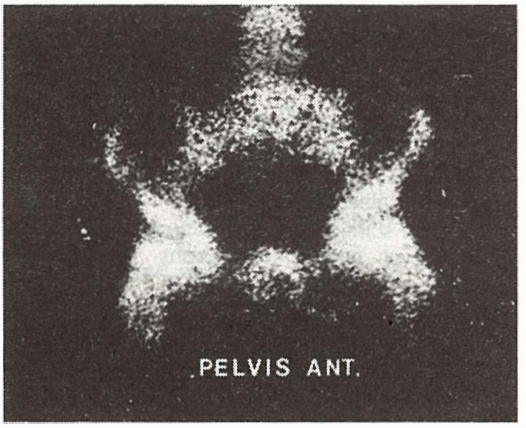
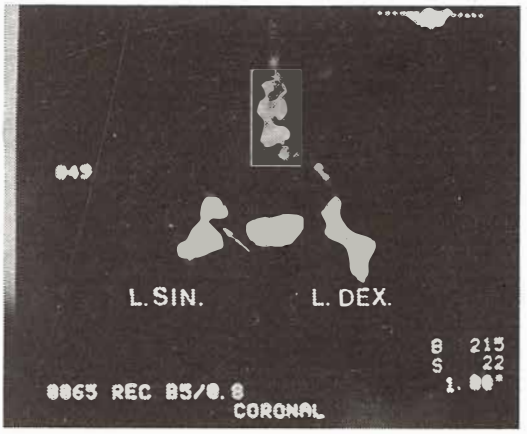




Fig. 2a – Planar scintigram of the pelvis – normal



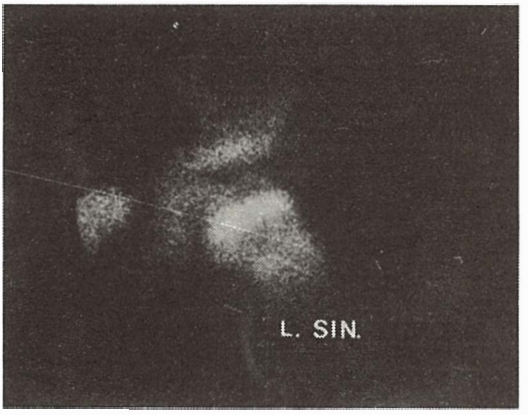




Fig. 2b – Pinhole scintigram of the left femoral head – normal

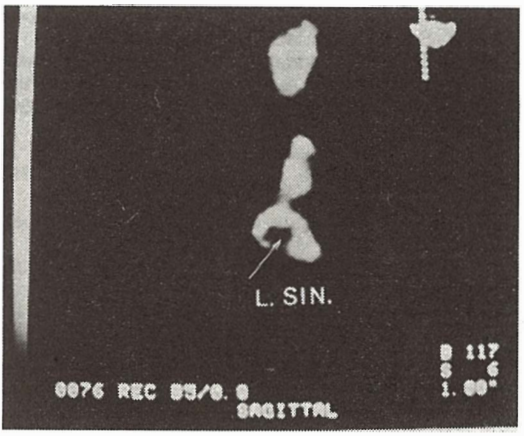



Fig. 1c, d, e – Three different SPECT images. More precise delineation of the photon deficient area and activity analysis of the growth plate with tomographic slices than with planar and pinhole scintigraphy

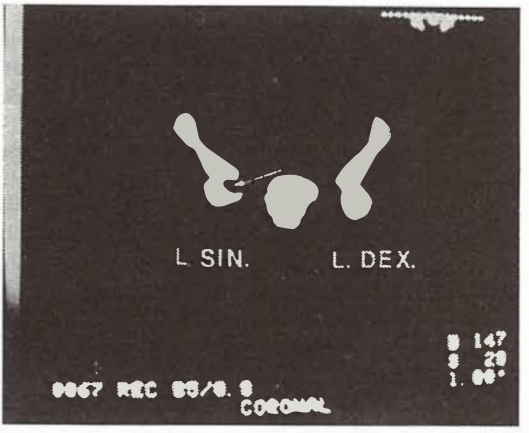



Fig. 2c – Coronal SPECT image, photon deficien area in the left femoral head (arrow)

In our investigation we compared only scintigraphic methods as unfortunately we had no opportunity to compare scintigraphic methods and NMR.

The comparison of scintigraphic methods proved SPECT to be the most sensitive of all. Performing this method we have had no false positive or false negative results.

Pin-hole scintigraphy was also highly sensitive (91%) since planar scintigraphy remained the least sensitive method.

We consider that using planar scintigraphy alone is not reasonable when the LCP disease is suspected if it is possible to use pin-hole scintigraphy. Taking into consideration the high sensitivity of SPECT, it does make sense to perform it in the cases where findings of pin-hole scintigrams are negative.

When using SPECT it is important to pay attention to possible appearance of artefacts caused by attenuation and depth dependent planar resolution of the rotating gamma camera. Artefacts may appear bacause of activity in the urinary bladder.

The physician interpreting scintigrams must be familiar with the physics of SPECT and tomographic reconstruction in order to be able to recognize possible artefacts and to explain the reasons of their occurence.

The choice of preprrocessing and butterworth is very important for the image quality. Different parameters will result in images of very varying quality.

SPECT is not only good in photon deficient area detection; this method allows also a better insight into growth plates, which is very important in choosing right therapy as for the prognosis of the disease.

Considering the high sensitivity of SPECT in our relatively small group of patients, we can indirectly conclude that SPECT sensitivity might be near to NMR sensitivity.

We are sure it is not possible to reach the sensitivity of 100% in SPECT technique as it happened in our small group of patients. We consider that in cases with negative pin-hole scans, where the clinical signs of the disease are present, it is necessary to perform additionally SPECT or NMR examination.

**Sažetak**

U dijagnostici Legg-Calve-Perthes-ove bolesti koriste se klinički i rentgenski pregled, scintigrafija, te odnedavno NMR. Pin-hole scintigrafija i NMR se smatraju najosjetljivijim metodama u detekciji aseptičke nekroze glave femura.

Cilj našeg istraživanja bio je da procijenimo osjetljivost SPECT-a u usporedbi s planarnom i pin-hole scintigrafijom zgloba kuka.

Kod 35 pacijenata smo učinili planarnu, pin-hole scintigrafiju te SPECT. Ispitanike smo podijelili u dvije skupine:

U prvu, koju su činili bolesnici s prisutnim kliničkim znacima bolesti, te drugu s bolesnicima koji su imali osim kliničkih simptoma i pozitivne RTG nalaze. Naši rezultati su pokazali da je SPECT najosjetljiviji među scintigrafskim metodama (100%). Pin-hole scintigrafija također je pokazala visoku osjetljivost (91%), dok je planarna scintigrafija bila najmanje osjetljiva.

Po našem mišljenju uputno je pin-hole scintigrafiju primjenjivati uvijek kada je prisutna sumnja na Perthesovu bolest. U slučaju negativnog rezultata korisno je učiniti SPECT koji predstavlja najosjetljiviju scintigrafsku metodu za detekciju ove bolesti. Ova metoda omogućuje ne samo detekciju »hladnih« zona već i bolji uvid u zone rasta što je vrlo važno za prognozu i liječenje bolesti. Iako je naša skupina ispitanika bila relativno mala, smatramo da naši rezultati ukazuju da je osjetljivost SPECT-a približna osjetljivosti NMR.

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# IN VITRO THYROID FUNCTION TESTS IN PATIENTS ON REGULAR HEMODIALYSIS: THE ROLE OF CHRONIC NONTHYROIDAL ILLNESSES

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**Abstract** – Thyroid function tests were performed in 22 patients on regular hemodialysis (RHD) with chronic nonthyroidal illnesses (NTI) – group I, 10 patients on RHD without chronic NTI – group II, and in 32 subjects of the control group. The groups were similar with regard to age, sex and nutrition, and patient groups with regard to duration of RHD and proportion of patients who received transfusion within last 7 days. Group I had significantly ($p \leq 0,01$) lower levels of $TT_4$, $TT_3$ and TBG than group II. There was no difference in the levels of $FT_4$, $FT_3$ and TSH between patient groups. Group I had significantly lower levels of $TT_4$, $TT_3$, $FT_4$, $FT_3$ and TBG than the control grup. Group II had significantly lower levels of $TT_3$, $FT_4$ and $FT_3$ than the control group, but there was no difference in $TT_4$ levels, and serum TBG concentration was significantly higher than in the control group. There was no difference in $rT_3$ and TSH levels between patient groups and the control group. Chronic NTI could be an important factor for the observed variability of thyroid function tests in patients on RHD in previously reported data.

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**Key words:** hemodialysis, thyroid function tests, thyroid hormones

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**Introduction** – Diverse abnormalities of in vitro thyroid function tests in patients on regular hemodialysis (RHD) have been documented (1–25), although clinical experience and metabolic studies suggested that most of these patients were euthyroid (1).

There is overall agreement of low levels of total triiodothyronine ($TT_3$) (1–25), sometimes to the hypothyroid range (2,3). Total thyroxine ($TT_4$) has been found normal (4-9) or low (2,10-22) and total reverse triiodothyronine ($rT_3$) the same (5,6,20) or lower (14,19,23) than in the control group. Thyroxine binding globuline (TBG) serum concentrations were usually reported normal (7,10,11,12,19), but also low (8) or high (5,6). The levels of free hormones depended on method (26), and unbound analog assay gave consistently depressed levels of free thyroxine ($FT_4$) (17,21) and free triiodothyronine ($FT_3$) (8,17,18,21).

The aim of this study was to investigate the influence of nonrenal nonthyroidal illnesses (27) on in vitro thyroid function tests in patients on RHD.

**Patients and methods** – Thirty-two patients on RHD (dialysed 1-3 times a week for a mean period of 35.4 months, range 1-131) were divided into two groups regarding the presence of chronic nonthyroidal illnesses (27) (Table 1) and compared with age–, sex– and nutritionmatched control group consisting of 32 healthy subjects. All patients and controls were clinically euthyroid and none of them had palpable goiter. None of the patients nor controls had diabetes mellitus or received any medications known to influence thyroid function.

Group I: 22 patients with chronic nonthyroidal illnesses (15 males, 7 females, aged 56.5 ± 10.9 years) underwent RHD for 1-121 months (mean 40,8). Their mean body mass index (BMI) was 25.1 ± 3.2 kg/m$^2$, relative body weight (RTW) 99.8 ± 12.3% and fat percent (fat %) 22.3 ± 7.1%. Eight of them received transfusion within last 7 days.

Group II: 10 patients without chronic nonthyroidal illnesses (7 males, 2 females, aged 56.5 ± 14.5 years) underwent hemodialysis for 1-131 months (mean 39.1). Their mean BMI was 23.7 ± 4.2 kg/m$^2$, RTW 94.5 ± 14.9 % and $fat_{\%}$ 19.4 ± 8.6%. Three of them received transfusion within last 7 days.

There was no difference between patient groups regarding the age and number of patients

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Table 1 – Presence of chronic nonthyroidal illnesses in studied group of patients (n = 22)

| Chronic nonthyroidal illnesses | Number of diseases |
|---|---|
| 1. Angina, myocardial infarction | 1 |
| 2. Myocardiopathia chr. comp. | 7 |
| 3. Hypertensio arterialis | 9 |
| 4. Other cardiovascular problems | 8 |
| 5. Respiratory disease | 1 |
| 6. Neurological problems and cerebrovascular accidents | 5 |
| 7. Gastrointestinal problems | 4 |
| 8. Musculosceletal disorders | 2 |
| 9. Hepatitis | 1 |
| 10. St. post operatio neoplasmae malignae | 1 |
| Total | 39* |

*9 patients had two or more nonthyroidal illnesses

Table 2 – In vitro thyroid function tests in patients on regular hemodialysis with (group I) and without (group II) chronic nonthyroidal illnesses and in control group

| | group I n = 22 | group II n = 10 | control n = 32 |
|---|---|---|---|
| $TT_4$ nmol/l | 72.9 ± 20 0[ac] | 89.9 ± 20.1 | 91.5 ± 21.6 |
| $TT_3$ nmol/l | 1.03 ± 0.27[ac] | 1.27 ± 0.27[c] | 1.49 ± 0.36 |
| $FT_4$ pmol/l | 9.31 ± 2.85[c] | 9.99 ± 2.64[c] | 14.90 ± 3.45 |
| $FT_3$ pmol/l | 2.32 ± 1.09[c] | 2.79 ± 0.80[c] | 5.70 ± 0.99 |
| $rT_3$ nmol/l | 0.234 ± 0.084 | 0.233 ± 0.052 | 0.234 ± 0.058 |
| TBG mg/l | 20.5 ± 4.4[ac] | 26.0 ± 5.8[c] | 22.1 ± 5.4 |
| TSH mlJ/l | 3.53 ± 1.41 | 3.57 ± 1.25 | 3.59 ± 1.75 |

a – $p \leq 0.01$ group I vs. group II

c – $p \leq 0.01$ groups of patients vs. control group

who received transfusion within last 7 days. There were a few more females in group I.

Control group: 32 subjects (23 males, 9 females aged 56.5 ± 11.9 years) had mean BMI 23.7 ± 2.1 kg/m$^2$, RTW 96.0 ± 11.2 % and fat$_{\%}$ 23.8 ± 6.9 %.

Control group had the same age structure as patient groups I and II, but the proportion of females was somewhat higher than in group I and slightly lower than in group II. Although the differences in sex did not allow statistical analysis, the nutritional status of all groups seemed very similar.

Blood samples of patients on RHD were taken before heparin injection, after the longest period between two dialyses, and of control subjects after overnight fasting.

All analyses were performed by radioimmunoassay technique, using comercial kits ($TT_4$, $TT_3$ – Vinča, Yugoslavia; TSH – INEP, Yugoslavia; $rT_3$ – Biodata, Italy; TBG – Orbis, France; $FT_4$, $FT_3$ – Amersham, G. Britain).

Serum samples were stored at –20°C until the investigation of above compounds. All tests were performed in duplicate.

After analysis of variance, Student's nonpaired t-test was used to calculate the significance of difference of thyroid hormone between all groups.

**Results** – The results obtained are summarized in Table 2. The group of patients with concomitant chronic nonthyroidal illnesses (group I) had significantly ($p \leq 0{,}01$) lower levels of $TT_4$, $TT_3$, and TBG than the grup without them (group II). There was no difference in serum concentrations of $FT_4$, $FT_3$, $rT_3$ and TSH. There was no difference between the two groups of patients regarding the age and number of patients who received transfusion within last 7 days. There were a few more females in grup I.

Both groups of patients had significantly lower levels of $TT_3$, $FT_4$ and $FT_3$ than the control group. The mean value of $TT_4$ in group I was significantly lower than in the control group, but there was no significant difference between group II and the control group. The mean serum concentration of TBG in group I was significantly lower and in group II significantly higher than in the control group. There was no significant difference between both groups of patients and the control group regarding the levels of $rT_3$ and TSH.

**Discussion** – Low levels of $TT_3$ is a common feature of euthyroid sick syndrome, but levels of $TT_4$ depend on severity of underlying disorders (28). It is also observed that low serum $TT_4$ in nonthyroidal illnesses heralds a grave prognosis about the life of those patients (29).

It seems that disturbances in $T_3$ (10) and $T_4$ (4,5,6) metabolism in patients on RHD are related to the state of illness in general and those of $rT_3$ to be mediated by a factor or factors specific to the uremic state. The available data in the literature (1-25) demonstrate great variability in the incidence as well as in the severity of the thyroid hormone metabolism and in vitro thyroid function tests in patients on RHD. A well matched control group has been used to escape the influences of general factors of variability such as age, sex and nutritional status. However, notable variability of in vitro thyroid function tests

was still preserved in those patients. A normal level of serum $TT_4$ concentration in patients on RHD was usually found when normal general health of patients with no concomitant illnesses nor nutritional disturbances was reported (-84). A group of patients on RHD with the same features had also normal $T_4$ kinetic parameters (2). It was presumed that the reported disturbances in $T_4$ kinetic parameters and serum concentration levels might be related to the effects of concurrent nonthyroidal nonrenal illnesses in the patients studied (2). Center specific variations in thyroid hormone disturbances were also found (30), and it was suggested that at least partialy they could be attributed to the differences in metabolic control.

The investigated patients were dialysed in the same way, and there were no great differences in their metabolic control. Presence or absence of chronic nonthyroidal illnesses (NTI) was a dominant group caracteristic.

There is no difference between patient groups and the control group in total $rT_3$ levels. That confirms the opinion that $rT_3$ metabolism, as well as its serum concentration, is determined by the uremic state itself (5,6).

NTI markedly influence the levels of $TT_3$ and $FT_3$ and could contribute to the variability observed in the literature, but they are not dominant in establishing the differences in the control group.

The influence of NTI on $TT_4$ serum concentration is particularly interesting. The group of patients without them exerts no difference in $TT_4$ level when compared to the control group. The group of patients with NRNTI has significantly lower level of $TT_4$ than both, the control group and the group of patients without NTI.

The serum concentration of TBG in hemodialysis patients is merkedly influenced by NTI. Apart from the difference between patient groups, the group of patients without NTI had significantly higher and the group of patients with NRNTI significantly lower TBG levels than the control group. Sex differences are not essential because the group with the greatest proportion of females has the lowest levels of TBG.

Our results are not in disagreement with previous reports. Concomitant NTI could explain most dissimilarities observed in the literature, which could not be ascribed to the age, sex and nutrition differences nor to the previous medication. Several groups who have documented the presence of low $TT_4$ and TBG levels did not note the presence or absence of NTI (2,10-19,21,22).

**Sažetak**

IN VITRO TESTOVI TIREOIDNE FUNKCIJE KOD BOLESNIKA NA HRONIČNOM PROGRAMU HEMODIJALIZE: ULOGA HRONIČNIH NETIREOIDNIH BOLESTI

U literaturi postoji velika varijabilnost u tipu i stepenu poremećaja in vitro testova tireoidne funkcije kod bolesnika na hroničnom programu hemodijalize (HPHD). Da bi se ispitao uticaj pridruženih hroničnih netireoidnih bolesti (NTB) upoređen je nivo $TT_4$, $TT_3$, $rT_3$, TBG, $FT_4$ i $FT_3$ kod 22 bolesnika na HPHD sa hroničnim NTB (I grupa), 10 bolesnika na HPHD bez pridruženih NTB (II grupa) i 32 subjekta kontrolne grupe. Grupe su bile slične polne i starosne strukture i stepena uhranjenosti a grupe bolesnika su imale slično prosečno vreme na HPHD i proporciju bolesnika koji su u toku poslednjih 7 dana dobili transfuziju opranih eritrocita. I grupa bolesnika ima visoko značajno ($p \leq 0,01$) niže nivoe $TT_4$, $TT_3$ i TBG od II grupe. Grupe bolesnika se ne razlikuju značajno u nivou $FT_4$, $FT_3$, $rT_3$ i TSH.

I grupa bolesnika ima visoko značajno niži nivo $TT_4$, $TT_3$, $FT_4$, $FT_3$ i TBG od kontrolne grupe. II grupa bolesnika ima visoko značajno niži nivou $TT_3$, $FT_4$ i $FT_3$ od kontrolne grupe ali nema razlike u nivou $TT_4$ a serumska koncentracija TBG je značajno viša od one u kontrolnoj grupi. Grupe bolesnika se ne razlikuju značajno među sobom niti sa kontrolnom grupom u nivoima $rT_3$ i TSH.

Rezultati istraživanja ukazuju da su pridružene hronične NTB važan faktor varijabilnosti $TT_4$ i TBG kod bolesnika na HPHD.

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MEDICINSKI CENTAR U ZAJEČARU, SLUŽBA ZA NUKLEARNU MEDICINU

# PROCENA AUTOIMUNE STIMULACIJE ŠTITASTE ŽLEZDE TESTOM AKUMULACIJE 99m–Tc PERTEHNETATA

## EVALUATION OF AUTOIMMUNE STIMULATION OF THYROID BY 99m–Tc PERTECHNETATE UPTAKE TEST

Paunković N, Paunković J, Pavlović O

**Abstract** – Original modification of »short« (five minutes) 99m–Tc pertechnetate thyroid uptake test was applied for evaluation of autoimmune stimulation of the thyroid in immunogenic hyperthyroidism. Tracer was applied intravenously, and the uptake registered by computerized gamma camera; the results were presented in form of »normalized slope«. Data were compared with clinical evaluation, thyroid hormones and TSH receptor autoantibody levels. The following data were obtained: test was normal in control group (30 euthyroid persons); in Graves' disease patients (35 patients) test values were elevated (decreased by induction of remission); test was normal in 9 patients with disseminated thyroid autonomy. Comparing thyroid uptake results with thyroid hormones and TSH receptor antibodies levels we concluded that this test evaluated autoimmune stimulation rather than thyroid function.

**UDC:** 616.441-008.67-07:539.163

**Key words:** Graves' disease, thyroid function tests, technetium-diagnostic use

**Orig sci paper**

**Radiol Iugosl** 1991; 25:43–6.

**Uvod** – Fiziološki (TSH) i patološki (TSI – tireostimulantni imunoglobulini) stimulatori tireoidne funkcije utiču na akumulaciju jednovalentnih anjona (jodidi, perhlorat, pertehnetat) u štitnjači. Mogućno je vršiti procenu delovanja autoimunih stimulatora (TSI) u hipertireozi merenjem intenziteta tireoidnog »trapping« mehanizma intravenskim testovima akumulacije 99m-Tc pertehnetata ili jodida (I-132, I-123) u ranoj fazi (1,2,3,4). Oba ova testa imaju značajna ograničenja za rutinski rad: testovima akumulacije radiojoda ne meri se samo zahvatanje (»trapping«) jodida već i naknadna organifikacija joda, dok rad sa niskoenergetskim i kratkoživućim tehnecijumom zahteva brojne merne korekcije (za ekstratireoidnu aktivnost, sa slabljenjem prilikom prolaska gama zračenja kroz tkiva, za radioaktivni raspad, itd) (1,2,5).

Mi smo razradili test za merenje akumulacije 99m-Tc pertehnetata kojim smo izbegli pomenute korekcije te ga na taj način prilagodili za rutinski rad.

**Materijal i metode** – a) Test akumulacije 99m-Tc pertehnetata u štitnjači – Koristi se standardna scintilaciona gama kamera (mi koristimo Pho/gamma IV, Searle, USA) sa paralelnim kolimatorom opšte namene za tehnecijum. Nakon intravenske aplikacije 50-80 MBq 99m-Tc pertehnetata bolesniku u ležećem položaju, vrši se kontinuirano merenje radioaktivnosti nad štitnjačom i prikupljanje podataka na »on line« vezanom računaru u toku 5 minuta. Prethodno merenje radioaktivnosti ubrizgane doze na gama kameri nije potrebno. Nakon prikupljanja podataka konstruiše se krivulja akumulacije iz »regiona od interesa« nad štitnjačom (fitovana funkcijom najmanjih kvadrata komercijalnim programom) bez korekcije za ekstratireoidnu aktivnost. Izračunavanje tireoidne akumulacije tehnecijuma vršimo po formuli:

$$^{99m}TcU = \frac{SLOPE}{A} \times 1.000$$

Priraštaj (»slope«), izražen u radioaktivnim impulsima u sekundi, meri se u linearnom delu krive omeđenom graničnicima **A** i **B.** Graničnik **A** deli završetak »vaskularne faze« (trenutke akumulacije) od početka rane akumulacije, a graničnik **B** postavljamo na kraj linearnog priraštaja (najčešće oko 3 min) od graničnika **A.** Oznaka A u imeniocu obrasca predstavlja izmerenu radioaktivnost u opsegu koji zahvata graničnik **A** (u impulsima / 4 sekunde). Normalizacijom priraš-

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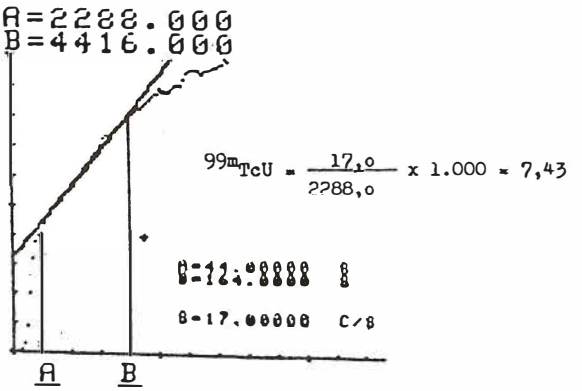
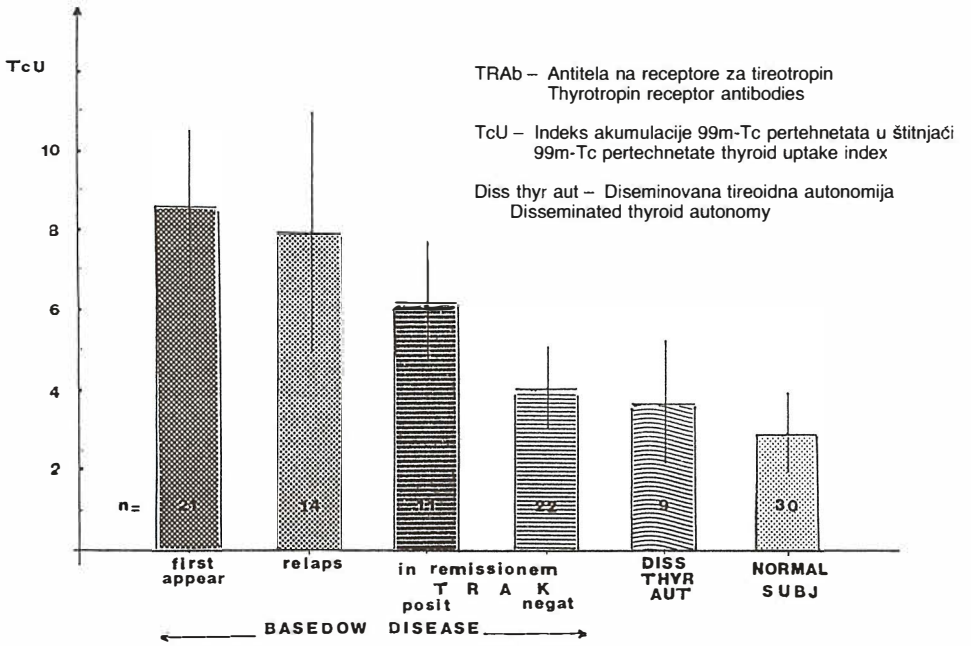



Slika 1 – Izračunavanje indeksa akumulacije 99m-Tc pertehnetata sa krivulje nad štitnjačom

Fig. 1 – Calculation of 99m-Tc pertechnetate uptake index from thyroid curve

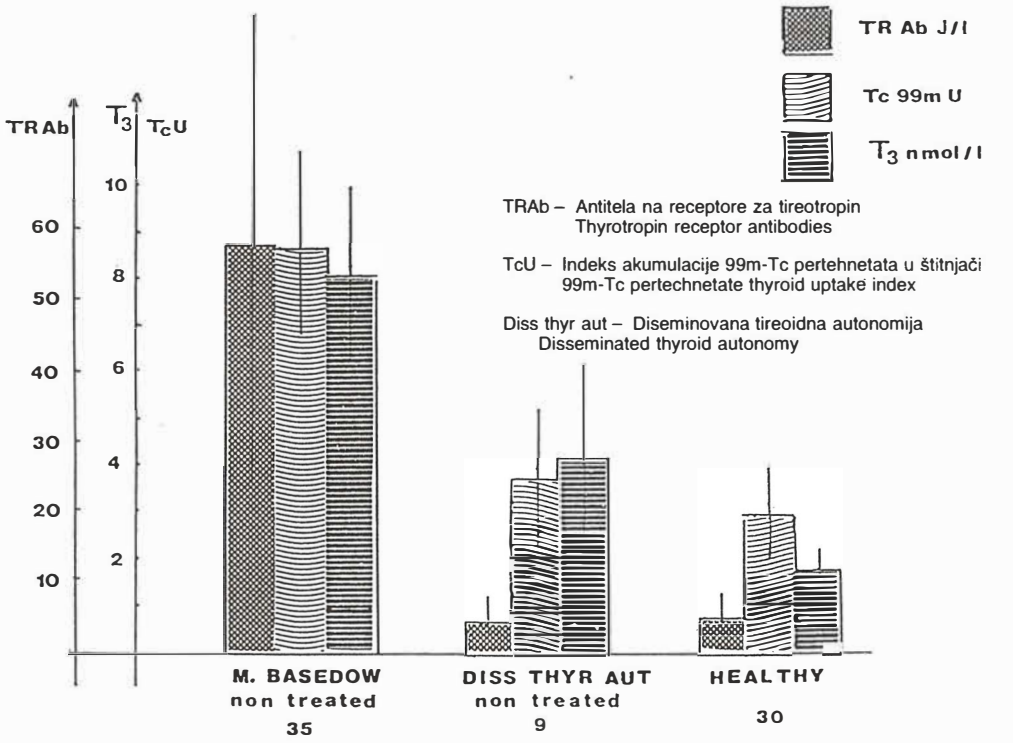



Slika 2 – Akumulacije 99m-Tc pertehnetata u ispitivanih osoba

Fig. 2 – 99 m-Tc pertechnetate thyroid uptake in investigated persons

taja početnom aktivnošću (SLOPE/A) dobija se neimenovani indeks koji iz praktičnih razloga množimo sa 1.000 (slika 1).

b) Ispitivane osobe – Test je primenjen kod 35 bolesnika sa nelečenom Bazedivljevom bolešću (21 novootkriven i 14 sa recidivom), 33 bolesnika sa istim oboljenjem u remisiji (25 lečenih metimazolom i 8 operativno), 9 bolesnika sa nelečenom diseminovanom tireoidnom autonomijom i 30 eutireoidnih osoba bez strume. Ispitivane grupe su zasnovane na osnovu kliničke procene (dva nezavisna endokrinologa), rezultata tireoidnih hormona i TSH (RIA) i receptorskih TSH antitela (radioreceptorski test, TRAK-assay, Henning).




Slika 3 – Koncentracije antitela na receptore za tireotropin i trijodotironina i vrednosti akumulacije 99m-Tc pertehnetata u hipertireozi

Fig. 3 – Thyrotropin receptor antibodies, $T_3$ concentrations and 99m-Tc uptake in hyperthyroidism

**Rezultati** – Rezultati testa akumulacije 99m-Tc pertehnetata u grupama ispitivanih osoba prikazani su na slici 2.

Vrednosti ovog testa su uporedno prikazane sa koncentracijama trijodotironina (kao parametar hiperfunkcije štitaste žlezde) i nivoima antitela na receptore za tireotropin (kao parametar autoimune stimulacije štitnjače) u bolesnika od nelečene hipertireoze (slika 3).

**Diskusija** – Testovi kojima se meri zahvatanje (»trapping«) jednovalentnih anjona (jodid, pertehnetat) od strane tireocita primenjuju se više godina u ispitivanju obolelih od hipertireoze. Merenje akumulacije radioaktivnog pertehnetata se najčešće vrši upoređivanjem aktivnosti nad štitnjačom u 5-oj i 20-oj minuti od intravenske aplikacije, uz korekciju za radioaktivni raspad, ekstratireoidnu aktivnost i atenuaciju u mekim tkivima vrata (3,4,5,6). Ponekad se koriste i vrlo složeni višeprostorni modeli (1,2,7). Modifikacijom koju smo mi primenili (tehnika »normalizovanog slope-a«) mogu da se izbegnu sve pomenute korekcije. Koristili smo merenje u najranijoj fazi (1-5 minuta od aplikacije) jer smo želeli da procenimo samo »trapping« mehanizam a ne naknadni promet kroz tireocite.

U literaturi postoji dosta podataka o kliničkoj vrednosti testova zahvatanja pertehnetata ili jodida. Postoje mišljenja da je prediktivna vrednost za recidiv hipertireoze ovakvog testiranja mala (6,8), ili nasuprot tome vrlo visoka (9), pa čak i da se dobija više informacija o intenzitetu tireoidne stimulacije od testiranja tireostimulantnih antitela (10).

Rezultati ovog ispitivanja pokazuju da su vrednosti testa rane akumulacije pertehnetata uvek povišene u nelečenoj imunogenoj hipertireozi (Graves-ova bolest) za razliku od bolesnika za koje se na osnovu kliničkih kriterijuma i negativnog nalaza antitela na TSH receptore smatra da imaju neimunogenu hipertireozu (diseminovana tireoidna autonomija). Kod obolelih od Gravesove bolesti u remisiji, nalaz testa akumulacije tehnecijuma ostaje povišen uglavnom kod onih

gde se i pored trenutnog eutireoidnog stanja ne normalizuje vrednost receptorskih TSH antitela (slika 2). Naše mišljenje da se testom meri autoimuna stimulacija a ne funkcija štitnjače potkrepljuje i paralelizam nalaza testa akumulacije pertehnetata i receptorskih TSH antitela a ne ovog testa i koncentracije $T_3$ (slika 3).

**Zaključak** – Razradili smo brz i jednostavan test za merenje akumulacije 99m-Tc pertehnetata u štitnjači.

Testiranjem obolelih od različitih vrsta i stadijuma hipertireoze potkrepili smo mišljenje da se njime meri autoimuna stimulacija tireoideje.

Ovakvo »in vivo« testiranje autoimune stimulacije obolelih od imunogene hipertireoze posebno je korisno za ustanove koje nemaju mogućnost za određivanje tireostimulantnih antitela (metodom generacije c-AMP u tireocitima »in vitro«).

**Sažetak**

Primenjena je sopstvena modifikacija »kratkog« (petminutnog) testa fiksacije 99m-Tc pertehnetata u štitnjači radi procene autoimune stimulacije štitnjače u imunogenoj hipertireozi. Obeleživač je aplikovan intravenski, registrovanje akumulacije je vršeno gama kamerom i računarom, a rezultati su predstavljani u vidu »normalizovanog slope-a«. Podaci su poređeni sa kliničkom evaluacijom, rezultatima tireoidnih hormona i receptorskih TSH antitela. Dobijeni su sledeći nalazi: test je normalan u eutireoidnih osoba kontrolne grupe (30 osoba); u obolelih od Graves-ove bolesti (35 bolesnika) dobijaju se povišene vrednosti (snižavaju se uvođenjem u remisiju); test je normalan kod obolelih od diseminovane tireoidne autonomije (9 bolesnika). Upoređivanjem sa koncentracijama tireoidnih hormona i antitela na receptore za tireotropin, zaključili smo da se opisanim testom meri autoimuna stimulacija a ne funkcija štitaste žlezde.

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INSTITUT ZA NUKLEARNE NAUKE, VINČA,
INSTITU ZA BIOLOŠKA ISTRAŽIVANJA
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# UPOREDNO PROUČAVANJE VEZIVANJA SKELETNIH $^{99m}$Tc–RADIOFARMACEUTIKA ZA PROTEINE HUMANOG SERUMA

## A COMPARATIVE STUDY OF Tc–99m–SKELETAL RADIOPHARMACEUTICALS PROTEIN BINDING IN HUMAN SERA

Vanlić–Razumenić N, Petrović J, Tomić M, Ajdinović B, Rastovac M

**Abstract** – The interaction of three Ty–99m–skeletal agents (PYP, MDP, and DPD) with human serum proteins was studed from two aspects: total protein binding (in vitro), and selective protein binding (in vivo and in vitro). Results for total protein binding: $^{99m}$Tc-PYP 77,98±2,50%; $^{99m}$Tc-MDP 62,23±1,93%; $^{99m}$Tc-DPD 47,94±2,50%, results representing mean values of five experiments obtained by three methods. So, the value of bone uptake. vas in the opposite relation with the extent of protein binding; the bone uptake of $^{99m}$Tc-PYP < $^{99m}$Tc-MDP < $^{99m}$Tc-DPD, whereas protein binding of $^{99m}$Tc-DPD < $^{99m}$Tc-MDP < $^{99m}$Tc-PYP. Selective binding: the main transporting proteins for $^{99m}$Tc-PYP are transferrin and to a smaller extent albumin; for $^{99m}$Tc-MDP the main transporting proteins are albumin and $\beta$1-globulin, while for $^{99m}$Tc-DPD there are antitrypsin and albumin.

**UDC:** 612.398.12:539.163

**Key words:** blood proteins, protein binding, technetium

**Orig sci paper**

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**Uvod** – Najviše korišćeni radiofarmaceutski preparati na bazi tehnecijuma za scintigrafiju skeleta su Tc-99m-kompleksi pirofosfata (PYP), metilendifosfonata (MDP) i dikarboksipropandifosfonata (DPD). Ustvari, u poslednje vreme pirofosfatni kompleks se sve manje koristi za vizualizaciju skeleta, već je našao primenu za detekciju infarkta miokarda i kao posrednik u obeležavanju eritrocita. Fosfonatni kompleksi se koriste za sken koštanog sistema, s tim što se $^{99m}$Tc-DPD brže akumulira u kostnom tkivu i daje bolji odnos akumulacije u kosti u odnosu na meko tkivo, dok $^{99m}$Tc-MDP daje bolji odnos akumulacije u leziji u odnosu na zdravu kost (1).

Budući da su pitanja mehanizma transporta i selektivne akumulacije u ciljnom tkivu još nerasvetljena, i da je ovo pitanje važno i proučavano od strane niza autora (2–8), tema ovog rada je proučavanje interakcije radiofarmaceutika sa proteinima krvi i povezivanje ove pojave sa lokalizacijom radiofarmaceutika u živom organizmu.

Cilj ove studije bio je ispitivanje interakcije pomenutih radiofarmaceutika sa transportnim proteinima krvi sa dva aspekta: određen je stepen vezivanja za ukupne proteine humanog seruma pomoću eksperimenata u in vitro uslovima, a takođe je ispitano selektivno vezivanje za pojedine klase proteina na osnovu eksperimenata u in vitro i in vivo uslovima.

**Materijali i metode** – U ovom radu korišćeni su radiofarmaceutski kompleti za obeležavanje sa Tc-99m, kao i eluat $^{99m}$Tc-generatora proizvodnje Instituta za radioizotope IBK Vinča.

Vezivanje za ukupne proteine je određeno pomoću tri metode:

1) taloženjem proteina dodatkom 10%-ne trihlorsirćetne kiseline i obračunavanjem procenta vezane radioaktivnosti u odnosu na unetu;

2) taloženjem proteina dodatkom perhlorne kiseline 0,8 mol/L;

3) dijalizom kroz membranu koja propušta molekule do 12000 daltona u toku 24 časa protiv hladnog fiziološkog rastvora (+4°C).

U ovim eksperimentima korišćeni su humani serumi sakupljeni od više pacijenata (»pulovani«) prethodno obeleženi $^{99m}$Tc-preparatom u odnosu 0,4 ml (0,3-lmCi), preparata + 4,6 ml seruma u toku 20 minuta na sobnoj temperaturi.

Selektivno vezivanje za proteine je ispitivano posle obeležavanja seruma in vitro na gore opisan način, a za određivanje in vivo, uzimani su uzorci po 5 ml krvi od pacijenata koji su prethodno primili preparat radi scintigrafske pre-

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trage. Vezivanje za pojedine klase proteina je analizirano pomoću elektroforeze na gelu agaroze po metodi Johansson-a (9).

Uzorci seruma u količini po 10 μl su nanošeni u 15 proreza na startu gela, pa je vršena elektroforeza u veronalnom puferu pH 8,4 uz potencijalni gradijent 20V/cm, jačinu struje 160 mA u toku 60–70 minuta. Po završenoj elektroforezi po 12 traka je isecano poprečno na pravac u kome je obavljena elektroforeza, radi merenja na brojaču, dok su preostale trake bojene amido-blackom radi identifikacije proteinskih klasa.

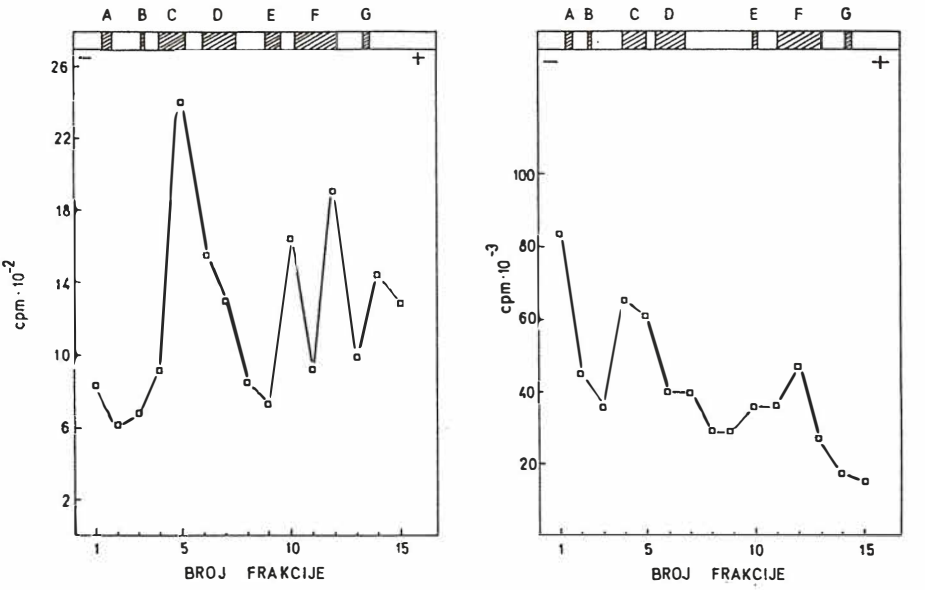
**Rezultati** – Srednje vrednosti određenih procenata vezivanja prikazane su u tabeli 1, dok su elektroforetogrami prikazani na slikama 1, 2 i 3.

**Diskusija** – U pogledu vezivanja na ukupne proteine krvi, iz dobijenih rezultata, prikazanih u Tabeli 1 se vidi da se $^{99m}$Tc-DPD u najmanjem stepenu vezuje za proteine, dok je poznato da je prihvat u kostnom sistemu kod primene ovog radiofarmaceutika najveći. Takođe $^{99m}$Tc-PYP, koji se najslabije vezuje za skelet od tri preparata koji su ovde upoređivani, pokazao je najveći

Tabela 1 – Vezivanje za ukupne proteine
Table 1 – Total protein binding

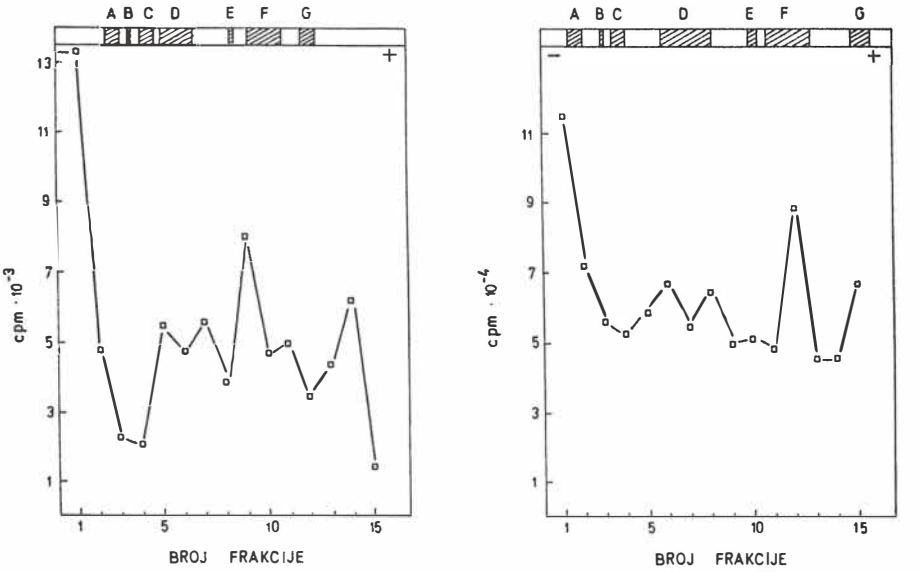
| KOMPLEKS<br>COMPLEX | TALOŽNE METODE<br>PRECIPITATION METHODS<br>PCA | <br><br>TCA | DIJALIZA<br>DIALYSIS | SREDNJA VREDNOST<br>MEAN VALUE |
|---|---|---|---|---|
| $^{99m}$Tc-DPD | 49,37±2,3% | 50,65±2,1 | 43,80±3,1% | 47,9±2,50% |
| $^{99m}$Tc-PYP | 88,26±1,1% | 89,71±1,3% | 55,97±5,1% | 77,98±2,50% |
| $^{99m}$Tc-MDP | 71,29±1,2% | 70,34±1,8% | 45,06±2,8% | 62,23±1,93% |

Skraćenice: PCA – perhlorna kiselina; TCA – trihlorsirćetna kiselina
Abbreviations: PCA – perchloric acid; TCA – trichloracetic acid



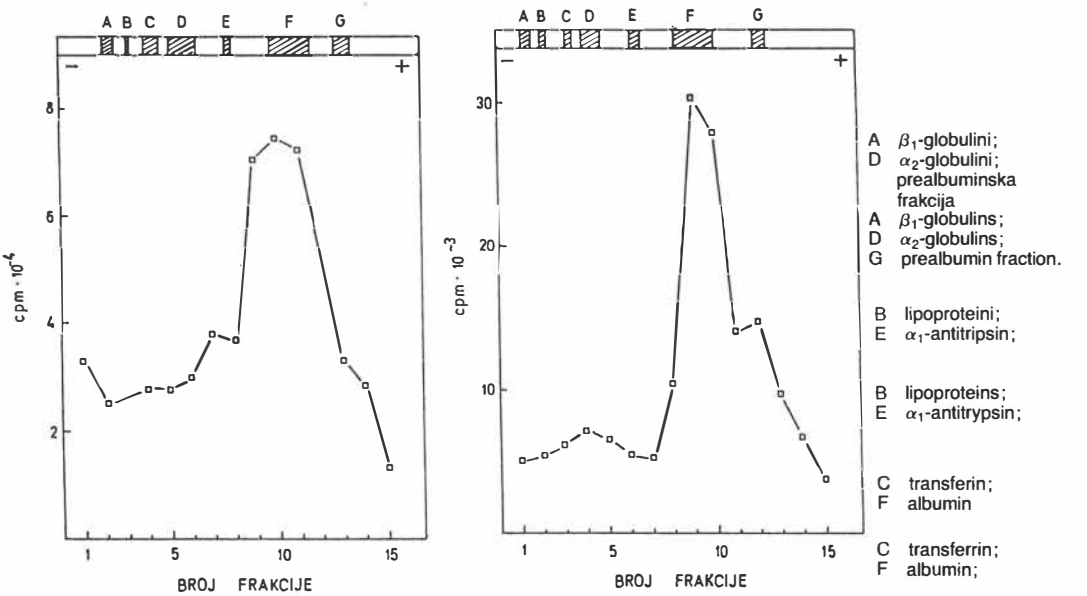

Slika 1 – Elektroforetogrami humanih seruma obeleženih sa $^{99m}$Tc-pirofosfatom: a) obeležavanje in vitro; b) serumi pacijenata kojima je dat preparat radi scintigrafije (uslovi »in vivo«)

Fig. 1 – Fractionation patterns of sera labelled with $^{99m}$Tc-PYP: a) Electropherogram of human serum labelled in vitro; b) Electropherogram of human serum obtained from patients after i.v. administration of the injection solution (»in vivo« conditions)




Slika 2 – Elektroforetogrami humanih seruma obeleženih sa $^{99m}$Tc-MDP: a) obeležavanje in vitro; b) serumi pacijenata kojima je dat preparat radi scintigrafije (uslovi »in vivo«)

Fig. 2 – Fractionation patterns of sera labelled with $^{99m}$Tc-MDP: a) Electropherogram of human serum labelled in vitro; b) Electropherogram of human serum obtained from patients after i.v. administration of the injection solution (»in vivo« conditions)




Slika 3 – Elektroforetogrami humanih seruma obeleženih sa $^{99m}$Tc-DPD: a) obeležavanje in vitro; b) serumi pacijenata kojima je dat preparat radi scintigrafije (uslovi »in vivo«)

Fig. 3 – Fractionation patterns of sera labelled with $^{99m}$Tc-DPD: a) Electropherogram of human serum labelled in vitro; b) Electropherogram of human serum obtained from patients after i.v. administration of the injection solution (»in vivo« conditions).

procenat vezivanja za proteine seruma. Dok je redosled stepena lokalizacije za ispitivane preparate $^{99m}$Tc-DPD > $^{99m}$Tc-MDP > $^{99m}$Tc-PYP, redosled stepena asocijacije za transportne proteine je obrnut: $^{99m}$Tc-DPD > $^{99m}$Tc-MDP > $^{99m}$Tc-PYP.

**Sažetak**

Proučavana je interakcija tri osteotropna radiofarmaceutika obeležena tehnecijumom (PYP, MDP i DPD) sa proteinima humanog seruma sa dva aspekta: vezivanje za ukupne proteine humanog seruma (posle interakcije u in vitro uslovima) i selektivno vezivanje za pojedine klase proteina posle obeležavanja in vitro i in vivo.

Proteinsko vezivanje je iznosilo (srednje vrednosti od po pet eksperimenata, dobijene pomoću tri alternativne metode): $^{99m}$Tc-PYP 77,98±2,50%; $^{99m}$Tc-MDP 62,23±1,93%; $^{99m}$Tc-DPD 47,94±2,50%. Tako je ustanovljeno da su vrednosti procenta akumulacije u skeletu obrnuto proporcionalne, t.j. u obrnutoj zavisnosti od stepena proteinskog vezivanja: dok procenat akumulacije raste u nizu $^{99m}$Tc-PYP < $^{99m}$Tc-MDP < $^{99m}$Tc-DPD, dotle procenat proteinskog vezivanja opada u nizu $^{99m}$Tc-PYP < $^{99m}$Tc-MDP < $^{99m}$Tc-DPD.

Selektivno vezivanje: glavni transportni proteini za $^{99m}$Tc-PYP su transferin i u manjoj meri albumin; za $^{99m}$Tc-MDP je albumin i u manjoj meri $\beta_1$-globulin; za $^{99m}$Tc-DPD antitripsin i albumin.

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# RADIOTHERAPEUTICALLY-INDUCED DETERIORATION OF IMMUNOLOGICAL DISTURBANCES IN LUNG CANCER PATIENTS

Vučković-Dekić Lj, Stanojević-Bakić N, Šušnjar S, Frim O

**Abstract** – The parameters of both cellular and humoral immunity were tested in 27 patients with unresectable non-small cell lung cancer prior to therapy, and in 13 of them who underwent radiotherapeutical treatment (average dose of 45-60 Gy in 22-30 fractions), immediately after the therapy. Almost all parameters of general immunocompetence were significantly altered in patients before therapy, when compared to the controls. The significant decrease of T cells'number and their function, and the significant increase of mononuclear phagocytes, were found in radiotherapeutically treated patients when compared to their results before therapy. The concentrations of circulating immunoglobulins and immune complexes remained unchanged. These results show that the irradiation affects cellular immunity profoundly, indicating that the immunorestorative therapy should be attempted in these immunocompromised patients.

**UDC:** 616-24-006.6:615.849:616.155.32

**Key words:** carcinoma non-small cell lung-radiotherapy, immunity cellular

**Orig sci paper**

**Radiol Iugosl** 1991; 25:51–6.

**Introduction** – Cancer is a disease associated with immunodeficiency, which is the result of both host immune system and tumor-derived immunosuppressive factors (1). This immunodeficiency progresses with the stage of the disease (2, 3). Patients with solid tumors often have defects in celullar immunity (4). Several studies dealing with immunologic investigations in lung cancer patients have been reported, some of them with contradictory results (5-8). As T lymphocytes are highly sensitive to irradiation (9-11), further aggravation of initial immunosuppression in patients receiving radiation therapy is probable. However, we found little evidence concerning the effect of irradiation on general immunocompetence in lung (12) and other cancers (13). In the current study, we attempted to evaluate several immunologic parameters of both celullar and humoral immunity in lung cancer patients prior to and immediately after radiotherapeutical treatment.

**Materials and methods – Patients** – 26 patients (44-70 years old, average age 57 years) with unresectable non-small-cell lung cancer (central localization) were included in this study; all were under no treatment when tested for their general immunocompetence. Thirteen of them were planned for radiotherapy only. They were treated with external radiation-photons energies of 10 MV (Linac), daily dose of 2 Gy to the total dose of 45-60 Gy, five times per week. We used treatment technique of two opposed parallel fields, encompassing the primary tumor with 2 cm margin and a part of the mediastinum. Both fields were treated daily. Chest x-rays and CT scans were used in treatment planning. Immediately after the radiotherapeutical treatment, these patients were tested for the same immunological parameters as before therapy.

**Controls** – The parameters of general immunocompetence were evaluated in 46 healthy volunteers, sex and age matched.

**Immunological testing** – The following parameters of general immunocompetence were evaluated in each patient and control person:

T lymphocytes – The relative and absolute numbers of total(E-RFC) and »active« (A-RFC) T-cells in peripherial blood were evaluated by rosetting with sheep erythrocytes (14). The reactivity of T-cells (TLyT) was evaluated by their proliferative response to mitogen phytohaemag-

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glutinin (PHA), using the method of Spužić et al. (15).

B lymphocytes – The relative and absolute numbers of B cells (YC-RFC) in peripherial blood were evaluated by rosetting with yeast particles coated with complement (16). The concentrations of circulating immunoglobulins – IgA, IgG and IgM were evaluated by radial immunodiffusion in agar gel (17). The concentration of circulating immune complexes (IC) was measured using PEG technique (18).

Mononuclear phagocytes – The percentage and absolute numbers of peripheral blood monocytes (MPh) were evaluated using the method of Vujanović et al. (19), and their yeast particles' phagocyting capacity (IPh) by the same technique.

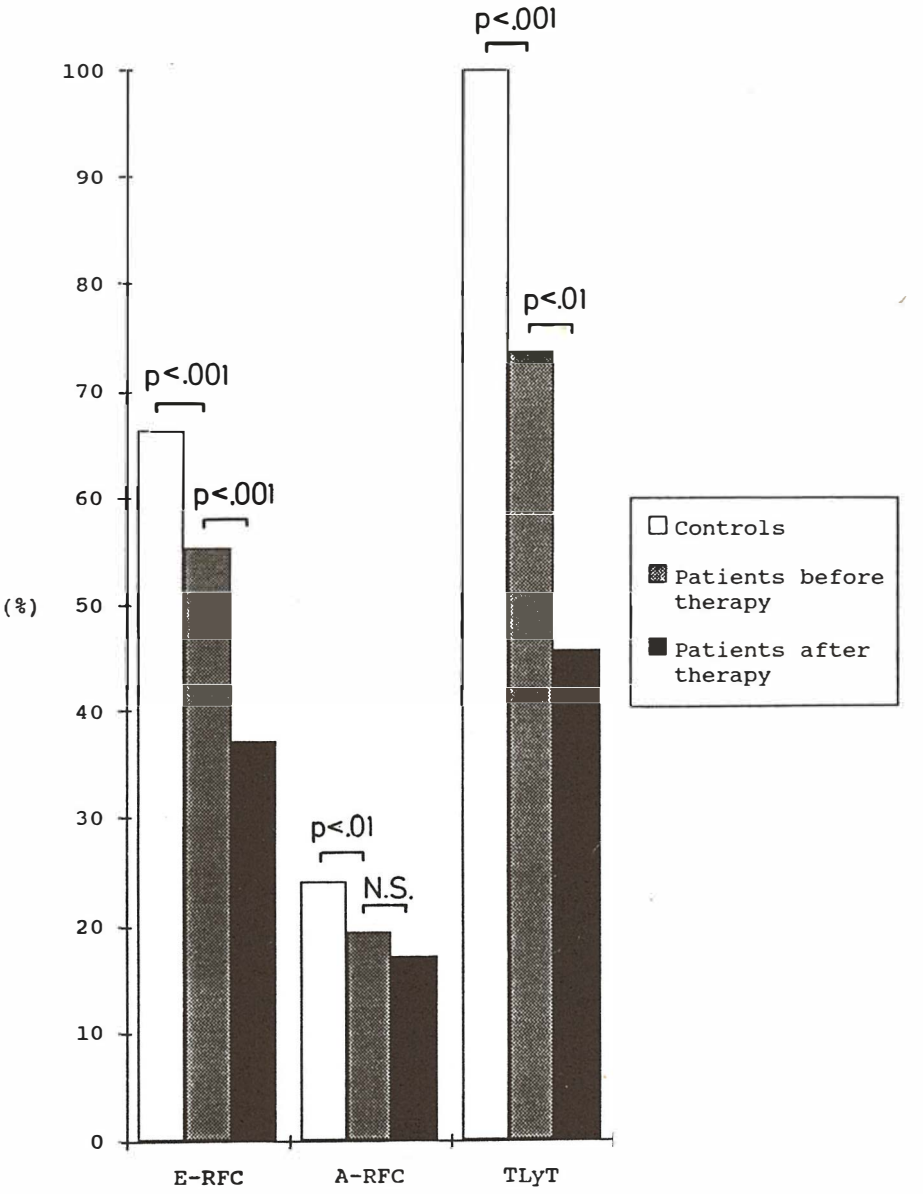


Fig. 1 – The percentage of total T lymphocytes (E–RFC) and »active« T lymphocytes (A–RFC) and their PHA – induced proliferative response (TLyT) in patients and controls (N.S. = not significant)

Data analysis – Statistical analysis of data was done with Student's t test.

**Results** – The significant decrease ($p < 0.001$) of total T cells' number was found in patients even before therapy. At the end of radiotherapy, these values were significantly ($p < 0.001$) lower, when compared to the same results before therapy (Fig. 1).

The percentage of »active« T cells was lower in patients than in controls ($p < 0.01$) and remained unchanged during the therapy (Fig. 1). The PHA-induced proliferative response of lymphocytes was decreased in patients before therapy ($p < 0.001$). These values were significantly ($p < 0.01$) decreased after radiotherapy (Fig. 1).

The B cells' number was significantly ($p < 0.001$) lower in patients than in controls; it was

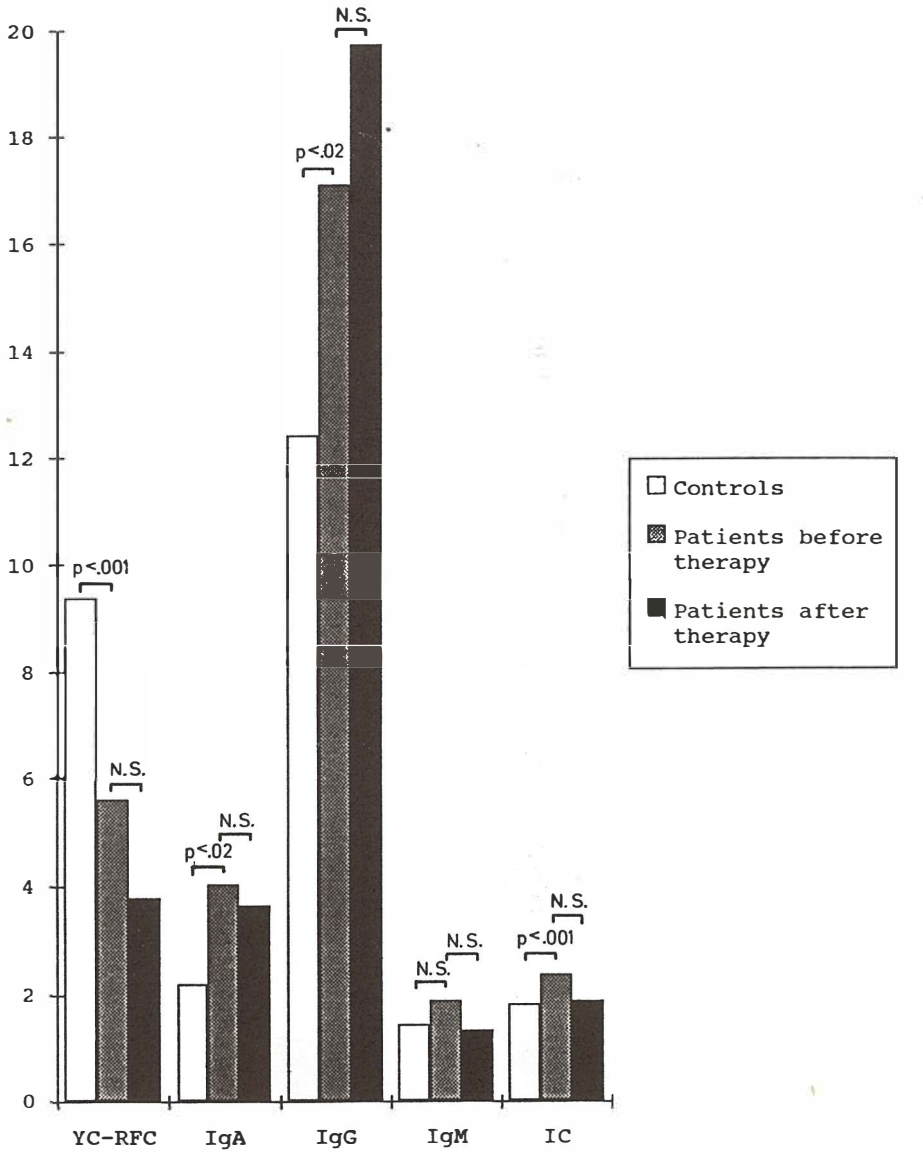


Fig. 2 – The percentage of B lymphocytes (YC–RFC) and concentrations of serum IgA, IgG, IgM and immune complexes (IC) in patients and controls. (N.S. = not significant)

slightly decreased in these patients after irradiation (Fig. 2). The concentrations of circulating IgA, IgG and immune complexes, all being significantly higher ($p < 0.02$, $p < 0.02$ and $p < 0.001$, respectively) in patients than in controls, remained high after therapy. Only the IgM values were similar in all three groups tested (Fig. 2).

The percentage of mononuclear phagocytes was significantly ($p < 0,001$) higher in patients than in controls; these values were even higher ($p < 0.001$) in radiotherapeutically treated group. The phagocytic activity of these cells was high in all patients before and after therapy (Fig. 3).

**Discussion** – All patients included in this study had gross immunologic alterations at the time of diagnosis. These alterations refer to both cellular and humoral immunity. Several previous

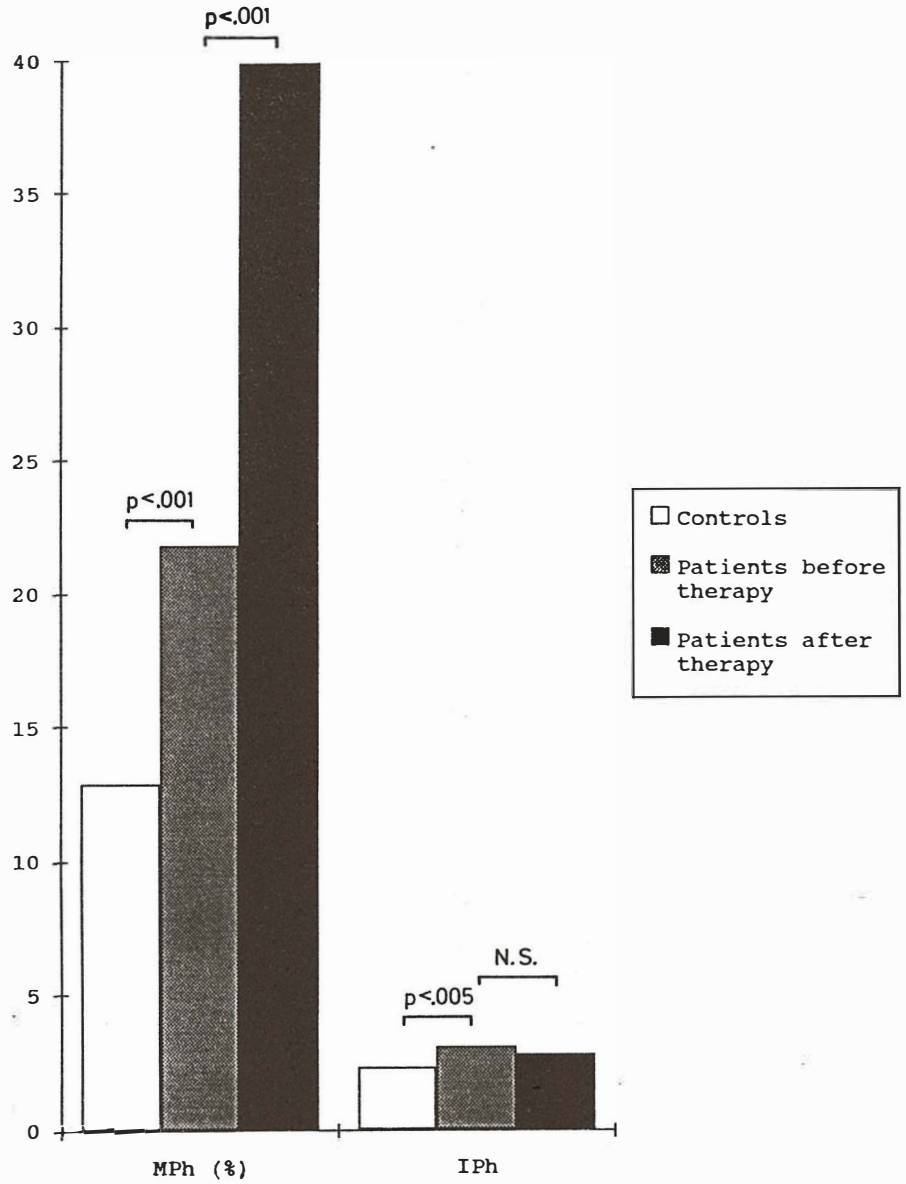


Fig. 3 – The percentage of mononuclear phagocytes (MPh) and index of phagocytosis (IPh) in patients and controls. (N.S. = not significant)

reports gave evidence of altered immune reactivity in lung cancer (5-8,20); some of them insist on restoration of depressed critical lymphoid elements by immunotherapy (21,22).

Radiotherapy caused more profound immunologic disturbances in our patients, the cellular immunity being affected to a greater extent. This is in agreement with earlier reports of deleterious effect of irradiation on immunocompetent cells (23-26). It should be noted that in all patients parts of mediastinum and thoracic duct were in the field of irradiation, so that the radiosensitive lymphocytes were exposed to its harmful effect directly. If lymphocytes mediate rejection of tumor cells, as they do with solid tissue transplants, the initial immunoincompetence followed by its radiotherapy-induced progression would be associated with poor prognosis (27). Therefore, an effort either to prevent further deterioration or to restore the compromised immunocompetence in patients planned for cytoreductive therapy, should be made. Such an attempt is under way in our group (28).

**Sažetak**

POGORŠANJE IMUNOLOŠKIH POREMEĆAJA U BOLESNIKA SA KARCINOMOM PLUĆA IZAZVANO RADIOTERAPIJOM

Parametri opšte ćelijske i humoralne imunosti su određivani u 27 bolesnika sa neoperabilnim planocelularnim karcinomom pluća pre terapije, i u 13 od njih koji su bili podvrgnuti radioterapiji (45-60 Gy u 22-30 seansi), odmah posle terapije. Većina parametara opšte imunosti je bila značajno izmenjena u odnosu na kontrolne osobe. Značajno smanjenje T limfocita i njihove funkcije, kao i značajno povećanje broja mononuklearnih fagocita, su nađeni u bolesnika koji su podvrgnuti radioterapijskom tretmanu. Radioterapija nije uticala na koncentraciju cirkulišućih imunoglobulina i imunokompleksa. Ovi rezultati pokazuju da radioterapija znatno produbljuje već postojeća oštećenja ćelijske imunosti u bolesnika sa kancerom pluća, što ukazuje na potrebu uvođenja imunorestorativne terapije kod bolesnika sa poremećenom imunošću.

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# CONCENTRATION OF MACRO AND MICROELEMENTS IN GLIOBLASTOMA AND COMPLETELY HEALTHY BRAIN TISSUES IN HUMANS

Huljev D, Milošević D, Rajković–Huljev Z, Graf D

**Abstract** – Concentrations of macro and microelements in tumorous (glioblastoma) and completely healthy brain tissue (autopsy material) from the same anatomic regions were analysed by NAA. Persons of similar ages (47 to 60 years) and sex (men), similar diet habits (same religion and customs), undergoing no therapy and taking no drugs, and resident in a specific geographical area (Zagreb), were selected for the study. Because »healthy« brain tissue in glioblastoma patients has not been available for analysis at the Institute for Tumors (which is obvious in view of the hazard for vital centres), completely healthy brain tissue required for comparison was obtained from persons who had suffered a violent death. Section material was obtained from the Forensic Medicine Institute of the Faculty of Medicine in Zagreb. Histologically neoplastic (21 patients) and healthy tissue (20 autopsy samples) were analysed. The tumorous to health tissue element concentration ratio (ug/g ppm) was the following: Zn (98 : 68 = 1.5 : 1); Fe (1145 : 341 = 3 : 1); Se (2.3 : 0.4 = 6 : 1); Co (0.09 : 0.03 = 3 : 1); Sc (0.007 : 0.002 = 3.5 : 1); Cs (0.07 : 0.01 = 7 : 1). When data were processed statistically, tumorous tissue was found to contain a significantly higher concentration of all the analysed chemical elements. Because of this radioactive selenium can be used for scintigraphic scanning of brain tumor sites.

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**Key words:** glioblastoma–analysis, elements

**Orig sci paper**

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**Introduction** – In unspoiled nature there is a balance between the concentration of macro and microelements in the environment, and their levels in the human body. If this balance is affected, a. g, by heavy metal contamination, various bodily functions can be upset. The potential role of macro and microelements in the origin and development of tumorous diseases, and the ever increasing pollution of the environment, suggest the need for basic research in this interesting area. The study of the relationship between macro and microelement concentrations, and tumorous diseases development, was meant to provide an insight into the possible correlation between the increased or decreased concentration of such elements in tumorous tissue as compared with the surrounding normal (or commpletely healthy) analogous tissue.

In terms of their importance for the human body, macro and microelements can be divided into four groups: a) essential (Fe, I, Cu, Zn, Mn, Co, Mo, Se, Cr and Sn); b) probably essential (Ni, F, Br, As, V, Cd, Ba and Sr); c) unessential (Al, Sb, Hg, Cd, Ge, Si, Rb, Ag, Au, Pb, Ti, etc.) and d) toxic (As, Pd, Cd, Hg, Be). Unessential and toxic elements enter the body through contact with the environment. All elements are toxic, but only those which are toxic in very low concentrations are classified as such. Each of the essential chemical elements can induce pathological conditions if taken in a concentration which upsets its physiological level in the body. If essential elements are present in the body in a homeostatic balance, the body is usually healthy.

The body obtains chemical elements by ingestion of food and water. In most cases the body obtains a sufficient amount of biogenic elements by normal diet, because the requirements are relatively low, and the needed concentrations are mainly present in a balanced environment (air, water, soil, vegetation) in adequate amounts.

If the established macro and microelement balance between the environment and living organisms is upset by intensive industrial and agricultural development, the content of organic and inorganic matter in our food should be monitored frequently (1). In this way one can discover in due time whether the body receives an increased or a reduced amount of individual elements. The disturbances which may develop can induce an extensive range of diseases. Such disturbances can be prevented in their initial phase by timely detection and by taking respective steps (addition or reduction). If, for example,

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the body gets a reduced amount of selenium in the diet, and if the selenium serum level drops to one–fourth of the required concentration, this can lead, over time, to the development of conditions such as arthritis, cardiac muscle weakening, multiple sclerosis, etc (2, 3, 4).

In urban environments where food stuffs from all over the country and the world are distributed, people receive in their diet amounts of various elements which differ from the level of such elements in food grown in the local environment. This reduces the possibility of accumulation of loss of some essential elements due to food intake. Drinking water awailable from a greater geographical area mainly contains a constant concentration of chemical elements, and it is consumed by populations of such areas. Because of the relatively high quantities drunk daily, water is a very important source of quite a few elements. Because of this, water has to be monitored continuously in order to establish whether it contains sufficient amount of essential elements as well as in order to establish possible surpluses or shortages which may lead to specific disesases.

Tumors are actually diseases involving multifactorial causes, and a tumorous disease should therefore be understood as a complex condition involving several possible causes, whereby different factors may predominate even in one and same tumorous disease. It is not easy to asume the role played by macro and microelements in the development of such disease, although it is generally being considered that they may be involved in one of the links in the chain of their origin.

One of the key issues regards the functions of metals in the body. Their most important role is related to metabolic chemical processes in the body, and to enzymes and nucleic acids. Some metals can stabilize, and others may destabilize the tertiary and quaternary structure of RNA and DNA molecules. Because of this, many trace elements are involved in the transfer of genetic information. One of the mechanisms underlying the development of pathological processes possibly induced by macro and microelements would involve the replacement of a »right« element by a »wrong« one at a key site in the enzyme, RNA or DNA molecule (5). The knowledge of normal and pathological levels of individual elements in helathy and deseased tissues, respectively, is also very important (6, 7, 8).

Some tumors contain higher levels of macro and microelements (9), as compared to the surrounding healthy tissues; in others this level may be reduced (6).

All this suggests non only the complexity of the relationship between tumors and element concentrations, but also the very pronounced albeit not entirely explained role of such elements in tumor development. Glioblastoma is the most frequent neuroectodermal brain tumor; in terms of malignancy, it shares the first position with medulloblastoma. It occurs exclusively in the mature age, mainly in the deep regions of the cerebrum hemispheres. It grows wery rapidly and may involve the entire hemisphere in a short time. It is made up of immature glia cells displaying different degrees of differentiation. It is particularly distinguished by its propensity to bleeding, in which case it may rapidly become enlarged and, by exerting pressure on the surroundings, cause clinical symptoms. It very often recurs, and may metastasize through liquor to other parts of the CNS (10).

**Material and methods** – For our study we had to obtain samples of completely healthy brain tissue in order to compare their microelement content with that of tumorous tissue (glioblastoma). Samples of healthy tissue were obtained directly during autopsy, at the Forensic Medicine Institute of the Faculty of Medicine in Zagreb, of persons who had suffered a violent death. Thus, the samples were entirely random, and obtained from persons with non anamnestic clinical or pathoanatomic disease, especially of the brain. Glioblastoma, the most frequent brain tumor, was used to test tumors; the intraoperatively obtained samples were immediately dehydrated and irradiated in a TRIGA nuclear reactor (9). In order to provide for an adequate distribution of age matching the age of most frequent glioblastoma occurrence, the persons selected for comparison in the violent death group were 47 to 60 years old.

Samples of tumorous and healthy tissue were irradiated together with the standard (beef liver 1577 NBS). Twenty–one tumorous and 20 healthy brain tissue samples were processed. Glioblastoma surgery often requires extensive resection, which is sometimes possible only as a palliative measure because of the proximity of vital CNS structures. In other words, the surgeon has to remove tumorous tissue without encroaching upon healthy or surrounding tissue. This is why the comparison was carried out against healthy tissue obtained from persons who had suffered a violent death, as already mentioned,

presenting an age distribution similar to that of the tumor patient group.

**Results** – Table 1 reviews only the results obtained by analysis of macro and microelements in tumorous and healthy brain tissues of persons living in one and same geographical area (breathing the same air, drinking almost identical water, and eating partly food grown on soil of a similar geochemical structure), and following similar habits (eating pork and other kinds of meat). In addition, these were persons of similar age, same sex, and taking no medication. The data were statistically processed by the Student t test of two arithmetic means.

**Discussion** – The results obtained show a significant Fe accumulation in tumorous brain tissue as compared with healthy tissue. The propensity of glioblastoma to vascularization and bleeding can probably explain part of this higher Fe level. Of course, this does not exclude a specific Fe role in the metabolism of enzymes and proteins required for tumor origin, or for its maintenance and growth.

We also established an unexpectedly higher level of Se in tumorous brain tissues as compared with healthy tissue. Because of this, some investigators have suggested the use of radioactive Se in brain tumor detection. The incidence of all human tumors is considered to be higher in areas with reduced selenium soil levels (4, 11). If the concentration of selenium in the diet is adequate, such diet can improve the body's defences against cancerogens. Studies have confirmed the reduction of cancerogenesis by the potent antioxidative effect of selenium compounds; they have also shown that antioxdiants can inhibit the first critical oxido–reductive reaction required for tumor development (13).

Zinc (Zn) also accumulates in brain glioblastoma. According to some reports, some tumors can be inhibited by zinc chortages. As assumed, tumorous tissue competes for Zn available to the body. Healthy tissue of the prostate abounds in zinc. Tumorous tissue contains a lower level of zinc as compared healthy tissue. This is explained by the incorporation of zinc into metalloenzymes which are synthesized at an accelerated rate by the tumorogenic process. Tumorous

Table 1 – Concentration of macro and microelements in tumorous (glioblastoma) and healthy brain tissue of persons living in the Zagreb area (autopsy samples). The results are given in $\mu$g/g(ppm), dry weight. Statistical processing of Zn, Fe, Se, Co, Sc and Cs composition data for tumorous and healthy human brain tissue.

| Element (student t–test) | | Tumorous tissue (21 samples) | Healthy tissue (20 samples) | p |
|---|---|---|---|---|
| | | Zagreb area; dry weight ($\mu$/g=ppm) | | |
| Zn | $\bar{X}$ – arithmetic mean | 98.0 | 67.6 | |
| | R – range | 50 - 270 | 45 - 90 | 0.01 |
| | $S\bar{X}$ – standard error | 10 | 4.0 | |
| Fe | $\bar{X}$ – | 1145.0 | 341.0 | |
| | R | 400 - 2770 | 150 - 550 | 0.001 |
| | $S\bar{X}$ | 118 | 33 | |
| Se | $\bar{X}$ | 2.3 | 0.4 | |
| | R | 2.1 - 2.9 | 0.3 - 0.5 | 0.001 |
| | $S\bar{X}$ | 0.06 | 0.05 | |
| Co | $\bar{X}$ | 0.09 | 0.03 | |
| | R | 0.001 - 0.2 | 0.001 - 0.004 | 0.001 |
| | $S\bar{X}$ | 0.01 | 0.002 | |
| Sc | $\bar{X}$ | 0.007 | 0.002 | |
| | R | 0.002 - 0.014 | 0.0004 - 0.0027 | 0.001 |
| | $S\bar{X}$ | 0.0007 | 0.0002 | |
| Cs | $\bar{X}$ | 0.07 | 0.01 | |
| | R | 0.01 - 0.13 | 0.001 - 0.019 | 0.001 |
| | $S\bar{X}$ | 0.007 | 0.0016 | |

breast tissue contains six times as much zinc as the surrounding normal tissue (9). The liver and kidneys of cancer patients contain higher zinc concentrations that the same organs in healthy subjects. Urinary excretion of zinc in patients affected by malignant disease is much higher than in healthy persons. Radiotherapy also increases the zinc serum level.

Cobalt is found in all living beings, with no major differences between levels. It is known as an enzyme activator and it is an essential trace element for all living beings.

Strontium is probably an essential element. Out of the total amount of strontium in the human body, about 99% is found in bones. The levels are somewhat higher in the larynx, trachea and colon. Small amounts of strontium are thought to be required for bone and tooth hardness.

Antimony is not considered to be an essential microelement for humans, animals and plants. Higher antimony levels have been detected in damaged hearth tissue in cases of mycrocardial infarction. Comparison of antimony levels in tumorous and surrounding pulmonary tissues have detected no significant differences. The importance of antimony in living systems has not been studied adequately.

Cesium is an unessential chemical element found in many plants and animals, and in the soil. Interest in cesium has increased particularly after the detection of high amounts of this element in areas contaminated by the Chernobyl disaster.

The results show relatively very small differences of selenium concentrations in cancerous (glioblastoma) brain tissue (2.1-2.9 ppm (ug/g)). Selenium content in the brains of standard man's also different very little (0.3-0.5 ppm). The concentrations of Zn, Fe, Se, Co, Sc and Cs in cancerous tissue was higher than in the healthy tissue and the differences were sifnificant, which is in agreement with many investigators (10, 14, 15).

**Sažetak**

KONCENTRACIJA MAKRO I MIKROELEMENATA U GLIOBLASTOMU I POTPUNO ZDRAVOM TKIVU MOZGA U LJUDI

Metodom NAA određene su koncentracije makro i mikroelemenata u tumorskim (glioblastomima) i potpuno zdravim tkivima mozga (obdukcijski materijal) istih anatomskih regija. Odabrane su osobe slične dobne skupine (od 47-60 g) i istog spola (muškarci), sličnog načina prehrane (iste vjere i običaja) koje još nisu dobile nikakvu terapiju niti su uzimali medikamente i žive ili su živjeli u određenom geografskom lokalitetu (Zagreb). Budući da u Institutu za tumore u Zagrebu nije bilo moguće dobiti za analiziranje »zdravo« tkivo mozga od bolesnika s glioblastomom (što je razumljivo da se ne ugroze vitalni centri pacijenta) uzeta su za uspoređivanje potpuno zdrava tkiva mozga od osoba koje su umrle nasilnom smrću. Sekcijski materijal je dobiven od Zavoda za sudsku medicinu Medicinskog fakulteta u Zagrebu. Histološki neoplastično (21 uzorak) i zdravo (20 uzoraka) tkivo je analizirano. Odnos koncentracija ($\mu$/g=ppm) elemenata u tumorskom prema zdravom tkivu je slijedeći: Cink (Zn) (98 : 68 = 1.5 : 1); Željezo (Fe) (1145 : 341 = 3 : 1); selen (Se) (2.3 : 0.4 = 6 : 1); kobalt (Co) (0.09 : 0.03 = 3 : 1); skandij (Sc) (0.007 : 0.002 = 3.5 : 1) cezij (Cs) (0.07 : 0.01 = 7 : 1). Statistička obrada podataka pokazuje da tumorsko tkivo mozga sadrži signifikantno povišenu koncentraciju svih analiziranih kemijskih elemenata. Zbog toga se može radioaktivni selen upotrijebiti za scintigrafsko traženje lokaliteta tumora mozga.

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## FROM PRACTICE FOR PRACTICE

### CARDIOVASCULAR SYSTEM

### Case 1

Answer:

This is a DSA Dynamic Cavernosogram, a procedure in which dilute contrast medium is infused directly into the corpora cavernosa to demonstrate the penile venous drainage and abnormalities of the corpora. This investigation is most commonly indicated in the investigation of organic Erectile Impotence but is also of use in the investigation of post-traumatic vascular problems and congenital or acquired penile deformities, such as those which occur in Peyronie's Disease.

This particular illustration shows marked opacification of the penile venous drainage, both deep and superficial veins, during an infusion of contrast. The veins are enlarged and this indicates abnormal penile venous leakage. The penis is not erect. In a normal patient the veins seen on the control film get smaller or disappear during the infusion.

Venous leakage is now widely accepted to be a common cause of erectile impotence. If arterial and psychosocial causes of erectile impotence are excluded, by non—invasive testing and pharmacological provocation, venous leakage seems to be the most likely cause of impotence. Cavernosography indicates the type of surgical or radiological treatment.

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**Kontraindikacije:** preobčutljivost za ciprofloksacin; otroci in mladi v dobi rasti; nosečnost, dojenje; previdnost pri starejših bolnikih in poškodbah osrednjega živčevja.

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INSTITUT ZA NUKLEARNE NAUKE »BORIS KIDRIČ« – VINČA, INSTITUT ZA RADIOIZOTOPE »RI«
INSTITUT ZA UROLOGIJU, UKC BEOGRAD

# ISPITIVANJE KLINIČKE PRIMENJIVOSTI MONOKLONSKOG ANTITELA BG–9 U DIJAGNOSTICI TUMORA PROSTATE

## EXPLORATION OF CLINICAL APPLICABILITY OF MONOCLONAL ANTIBODY BG-9 IN DIAGNOSTIC OF PROSTATE TUMORS

Ivanović V[1], Petrović M[1], Starčević–Božović A[2], Petronić V[2]

**Abstract** – The main objective of this study is to estimate the clinical applicability of a monoclonal antibody BG–9 in the diagnosis of human prostate tumors using immunohistochemical PAP staining procedure on 188 various human tissue sections and byopsies. Our results revealed that BG–9 was reactive with 54/59 benign prostatic hyperplasia tissue section, staining the epithelial cells of the ductus and the glandular structures, and 22/22 primary prostate carcinoma tissue sections, staining the epithelial cells of neoplastic acini. Most of the other tissue sections of normal and tumor origin did not react with BG–9 including: 21 normal prostate sections, 24 other normal tissue sections, 8 benign and 30 sections of other malignacies. Cross–reactivity of BG–9 was observed in only an 9/24 sections on malignant melanocytes of melanoma tissue. According to our results, immunohistochemical staining pattern of BG–9 antigen expression in prostate tumors is very similar to that of PSA and PSAP, suggesting that it may be used as a substitute. In addition, BG–9 antigen has evident advantages revealing positive staining with prostatic ductal epithelium. Further studies are in progress to determine whether BG–9 antigen may be a new imunohistologic marker for ductal prostatic carcinoma.

**UDC:** 616.65-006.6-097

**Key words:** prostatic neoplasms–diagnosis, antibodies monoclonal

**Orig sci paper**

**Radiol Iugosl** 1991; 25:63–7.

**Uvod** – Zahvaljujući tehnologiji hibridoma za dobijanje monoklonskih antitela (MoAt), svake godine se u oblasti kliničke onkologije identifikuje izvestan broj novih Tumor–Specifičnih Markera (TSM–a). Ovi markeri predstavljaju površinske antigene ili druge ćelijske proizvode koji se eksprimiraju kod specifičnih vrsta tumora. S obzirom da je u našoj laboratoriji u Vinči savladana tehnologija hibridoma (1), koncentrisali smo svoje eksperimentalne planove na dobijanje novog TSM–a u našim uslovima.

Nedavno smo izolovali seriju novih MoAt fuzijom mišjih mijelomskih ćelija i splenocita BALB/c miševa imunizovanih intaktnim ćelijama humanog malignog melanoma. Naša prva predklinička ispitivanja su pokazala da od novodobijenih MoAt, samo antitelo označeno kao BG–9 selektivno reaguje sa post–operativnim tkivima tumora prostate (2). Iz literature (3, 4) je poznato da je Prostata Specifični Antigen (PSA) jedan od najčešće korišćenih TSM–a u kliničkoj dijagnostici (5). Ovaj antigen predstavlja pouzdan marker u praćenju toka i terapije karcinoma prostate kao i u prognozi ishoda ove bolesti (5). Iz tih razloga, u okviru ovog rada je detaljno ispitana imunohistohemijska reaktivnost BG–9 MoAt na većem broju post–operativnih tkiva i biopsija tumora prostate i upoređena sa drugim vrstama tumora i zdravih tkiva.

**Materijal i metode** – 1. Priprema FO–1 ćelija za imunizaciju: Kontinuirana linija humanih FO–1 ćelija malignog melanoma je dobijena od Dr.P. Fisher–a sa Kolumbija Univerziteta u New Yorku. Ova kultura, raste u monosloju i umnožena je u DMEM podlozi, Dulbecoos Modified Eagle Medium (Flow Labs, Škotska), u prisustvu 10% telećeg seruma (Institut »Ruđer Bošković«, Zagreb), 100 U/ml penicilina i 100 ug/ml streptomicina. Brojanje vijabilnih ćelija je vršeno »Trypan blue« ekskluzijom pomoću hemocitometra, a odlepljivanje pomoću 0,2% EDTA u PBS–u. Za prvu i drugu imunizaciju su korišćene intaktne ćelije fiksirane 0.1% glutardialdehidom inkubiranjem u PBS–u, 5 min. na sobnoj temperaturi.

Protokol imunizacije: prema Morganu (6), šest ženskih BALB/c miševa od 7 nedjelja, soja AnNCR/$F_6$ (Vojnomedicinska akademija, Beograd) je imunizovao intraperitonalno sa $1X10^7$ fiksiranih FO–1 ćelija po mišu na dan 0 i na 7 u kompletnom Freund–ovom adjuvansu. Treća imunizacija je rađena 37–og dana koristeći

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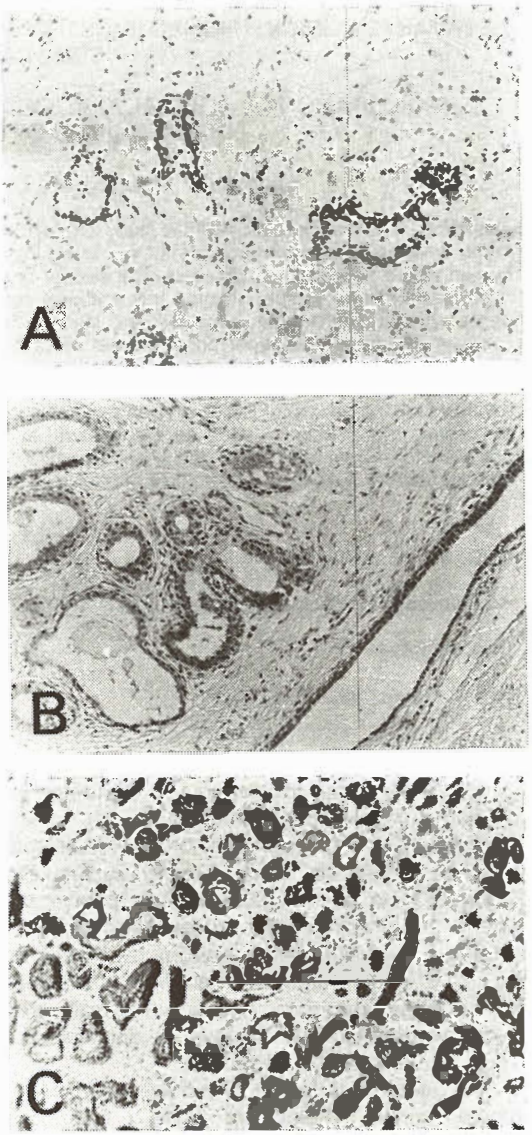
$5X10^6$ nefiksiranih ćelija po mišu u PBS–u, intravenski i intraperitonalno.

3. Fuzija i kloniranje : fuzija je rađena 41–og dana koristeći ćelije slezine imunizovanih miševa i X63–Ag8–653 mišje mijelomske ćelije kao partnere u fuziji prema prethodno opisanom protokolu (2). Posle dve nedelje zapaženo je 243 otvora mikro ploča sa klonovima hibridoma koji su lučili MoAt. Naknadnim testiranjem RIA metodom u ćelijskoj suspenziji izabrana su 32 klona čija MoAt su pokazala visok afinitet za intaktne FO–1 ćelije. Ovi hibridomi su subklonirani na agaru i ponovo testirani na lučenje. Ukupno četiri klona označena kao BG–2, BG–8, BG–9 i BG–16 su nastavila da luče i rastu u kulturi ispoljavajući traženu stabilnost.

4. Poreklo humanog tkiva : Dijagnoze humanih tkiva korišćenih u ovom radu su prikazane u tabeli 1. Za imunohistohemijska ispitivanja su korišćena kako sveža tako i fiksirana tkiva dobijena post–operativno ili posle biopsija sa VMA, Instituta za radiologiju i onkologiju, Instituta za urologiju u Beogradu kao i Instituta za onkologiju u Sremskoj Kamenici. Većina zdravih tkiva je dobijena post–mortem iz formalinskih preparata sa VMA u Beogradu. Fetalna tkiva su dobijena od Dr.B.Garzičića iz Instituta za majku i dete u Beogradu.

5. Priprema tkiva : U našem radu su analizirana sveža fiksirana kao i fiksirana humana tkiva. Sveža tkiva su naglo zamrzavana na -70°C. Isečci od 5 mikrona su dobijeni pomoću mikrotoma na -27°C i fiksirani na staklenim pločicama pomoću 0.02% glutaraldehida u PBS–u. Parafinski isečci posle formalinskog–acetonskog ili etanolskog–fiksiranja su deparafinizirani 5 min. innkubacijom u ksilolu (Merck Nemačka), isprani sa 100, 90 i 70% etanolom i destilovanom vodom, a zatim tripsinizirani 10 min. na 37°C koristeći 0,1% tripsin u prisustvu 0.1% $CaCl_2$ (pH 7.8). Posle toga je tkivo isprano hladnom destilovanom vodom i PBS–om.

6. Imunoperoksidazno bojenje :je rađeno PAP metodom Dippold–a i dr. (7). Da bi se neutralisalo dejstvo endogene peroksidaze, sveža i deparafinisana tkiva su prvo izložena 0.5% $H_2O_2$ u metanolu i ispirana nekoliko puta u periodu od 20 min. sa 0.05 M TRIS/HCl pH 7.6. Sličan način ispiranja je rađen posle svake inkubacije. Tkivo je inkubirano 20 min. sa 3,3% zečijim serumom, a zatim još 20 min. sa MoAt supernatantima ili ascitima mišjeg porekla. Posle ispiranja od 10 min, tkivo je inkubirano sa zečjim anti-mišjim IgG-om (Dakoppatts, Danska). Posle toga je usledila 20 min. inkubacija sa mišjim PAP




Slika 1 – Immunoperoksidazno bojenje u prisustvu monoklonskog antitela BG–9 na humanom tkivu kriostatskih-nefiksiranih (K) ili formalinom-fiksiranih/parafinski ukalupljenih (FP) post-operativnih isečaka: a) Normalna prostata (K); b) Benigna hiperplazija prostate (FP), i c) Primarni karcinom prostate (FP). [Originalno uveličanje x 250] Za detalje vidi Materijal i metode.

Fig. 1 – Immunoperoxidase staining reactivity of monoclonal antibody BG-9 on unfiksed kryocuts (K) of formalin-fixed, paraffin-embedded sections (FP) of: a) Normal Prostate (K); b) Benign Prostatic Hyperplasia (FP) and c) Primary Prostate Carcinoma (FP) [Original magnification x 250] For details see Materials and Methods.

Tabela 1 – Imunohistohemijsko bojenje BG-9 antigena na ukupno 188 različitih humanih tkiva

Table 1 – Immunocytochemical staining of BG-9 antigen on 188 various human tissue sections

| **NORMALNA** | formalin/parafin |
|---|---|
| TIP TKIVA | POZITIVNI/UKUPNO |
| Prostata | 0/21* |
| Mozak | 0/1 |
| Pluća | 0/1 |
| Hijalina hrskavica | 0/1 |
| Poprečeno prugasti mišić | 0/1 |
| Testis | 0/4 |
| Bubrezi | 0/6 |
| Fetalna tkiva | 0/9 |
| * 6 nefiksiranih/krio isečaka | (0/45) |

| **BENIGNO OBOLELA** (nefiksirani/krio) | |
|---|---|
| Benigna hiperplazija prostate | 54/59* |
| Naevus pigmentosus verrucosus | 0/3 |
| Kerathosis seborrhoica acantosis | 0/2 |
| Dysplasia cistica mammae | 0/1 |
| Lymphadenitis granulomatosa | 0/1 |
| Vasculitis chronica | 0/1 |
| * 33 preparata su fiksirana: formalin/parafin | (54/67) |

| **MALIGNO OBOLELA** (nefiksirani/krio) | |
|---|---|
| Karcinom prostate | 22/22* |
| Adenokarcinomi (kolon i rektum, želudac, bubreg, endometrijum, žučna kesa) | 0/9 |
| Metastaza adenokarcinoma u mozak | 0/1 |
| Maligni schwannom | 0/2 |
| Ependimom | 0/1 |
| Planocelularni karcinomi (koža, larinks, rožnjača, pluća) | 0/9 |
| Bazocelularni karcinom kože | 0/2 |
| Karcinom testisa | 0/2 |
| Karcinom bubrega | 0/3 |
| * svih 22 su tretirani: formalin/parafin | (22/52) |

| **MALIGNI MELANOM** | | |
|---|---|---|
| Način tkivne preparacije | Pozitivno / Ukupno primarni | metastaza |
| Nefiksirani/krio | 4/8 | 0/1 |
| Krio/aceton | 2/2 | – |
| Formalin/parafin | 1/6 | 1/1 |
| Etanol/parafin | 1/6 | – |

kompleksom (Dakoppatts, Danska), 10 min. ispiranja, i 20–40 min. izlaganja 0.5 mg/ml diaminobenzidina (Sigma, SAD) u PBS-u koji je sadržao 0.1% $H_2O_2$. Posle pojave smeđeg obojenja, tkivo je isprano tekućom vodom. U našem radu sa BG-9 MoAt korišćeni su nerazblaženi supernatanti kao i razblaženja ascita pri koncentraciji 1 mg/ml. Kao pozitivna kontrola je korišćena komercijalno MoAt protiv PSA jednolančanog polipeptida približne molekulske težine od 34 Kd. Kao negativna kontrola korišćeno je Y7 MoAt mišjeg porekla, da bi se uporedio nivo nespecifičnog vezivanja odnosno prisustvo endogene peroksidaze.

**Rezultati i diskusija** – U cilju utvrđivanja kliničke primenjivosti MoAt BG-serije, četiri dobijena antitela su ispitana *in situ*. Za te svrhe je korišćena imunohistohemijska PAP tehnika kao prihvaćena predklinička metoda za određivanje specifičnosti monoklonskih antitela. Preliminarna imunoperoksidazna bojenja su pokazala da samo MoAt označeno kao BG-9 specifično reaguje sa malignim melanomom, kako sa svežim tako i prethodno fiksiranim tkivima (8). Izvršena je izotipizacija ovog MoAt imunoradiometrijskom metodom (9) i utvrđeno je da BG-9 predstavlja $IgG_1$, kapa izotip. U istom radu je zapaženo da postoji selektivna ukrštena reaktivnost sa 2/2 tkiva hiperplastične benigne prostate (8). Ohrabreni ovim rezultatima u okviru ovog rada nastavili smo sistematsku i detaljnu imunohistohemijsku analizu na ukupno 188 različitih humanih tkiva.

Tabela 1 sumira rezultate naših imunoperoksidaznih bojenja.

Očigledno a je da od 8 vrsta ispitanih normalnih tkiva, koja su uključila i veći broj uzoraka tkiva normalne prostate, nijedno nije reagovalo sa BG-9 MoAt (tabela 1). Primer negativnog bojenja za slučaj normalne prostate je ilustrovan na slici 1A. Treba istaći da je 6 uzoraka normalne prostate predstavljalo sveža, nefiksirana tkiva. Takođe je interesantno da se na listi negativno obojenih normalnih tkiva nalazi, osim bubrega i testisa, veći broj fetalnih tkiva. Ovaj podatak isključuje mogućnost da je BG-9 antigen onkofetalnog porekla. U nastavku rada smo ispitali 6 vrsta benignih tkiva i 9 vrsta malignih tkiva i utvrdili da jedino tkiva tumora prostate reaguju sa BG-9 i to 54/59 benignih hiperplazija prostate i 22/22 karcinoma prostate (tabela 1). Primeri pozitivnih bojenja tumora prostate su prikazani na slici 1B i 1C. Ova obojenja su veoma slična

bojenju PSA na identičnim uzorcima. Ona obuhvataju ćelije epitela žljezdanih struktura. Takođe je zapaženo, slično kao kod PSA, da intenzitet obojenja kod karcinoma prostate opada sa stepenom dediferencijacije ovih tkiva. Međutim, za razliku od PSA, u slučaju BG-9 antigena dolazi do pozitivnog bojenja i na ćelijama epitela izvodnih kanalića kod benigne hiperplazije prostate (Slika 1B).

Poznato je da površinski antigeni prisutni na tumorskim ćelijskim linijama koje se održavaju in vitro ne preslikavaju u potpunosti in vivo antigenski profil. S obzirom da su FO-1 ćelije malignog melanoma korišćene kao imunizacijski antigen, u daljem radu je ispitano i utvrđeno da 9/24 tkiva malignog melanoma pozitivno reaguje sa BG-9 MoAt. Ovaj rezultat ukazuje da se BG-9 antigen eksprimira in vivo kod ove vrste tumora. Međutim, ekspresija ovog markera nije podjednako zastupljena u svim ispitanim slučajevima svrstavajući BG-9 antigen u grupno-specifične markere malignog melanoma. Posebno treba istaći da kvalitet pozitivnog bojenja u našim ispitivanjima nije zavisio od prethodnog tretmana tkiva, ukazujući da BG-9 antigen nije podložan denaturaciji u prisustvu fiksacionih agenasa kao što su formalin, aceton ili etanol (tabela 1). Time se postiže dodatna prednost BG-9 MoAt u histopatološkoj dijagnostici, s obzirom da se omogućuje korištenje zaliha starih tkiva za retroaktivna ispitivanja.

Poznato je iz literature (3,4) da se u dijagnostici i prognozi tumora prostate za sada koriste markeri kao što su PSAP (Prostate Specific Acid Phosphatase) i PSA (Prostate Specific Antigen). Dok PSAP predstavlja enzim i to ortofosforni monoestar fosfohidrolize, PSA predstavlja jednolančani glikoprotein približne molekulske težine od 34 Kd. Utvrđeno je da se PSA eksprimira na ćelijama epitela žljezdanih struktura zdrave prostate kao i karcinoma prostate, a da nije zastupljen na drugim vrstama zdravih tkiva ni maligniteta.

Naši dosadašnji rezultati ukazuju da BG-9 antigen može da se upotrebi za slične svrhe kao PSA. Naša preliminarna biohemijska ispitivanja ukazuju da BG-9 antigen predstavlja heterodimer od 100 i 150 Kd (rezultati nisu prikazani). S obzirom na ovu činjenicu, kao i na podatak da sa BG–9 reaguju i ćelije epitela izvodnih kanalića, pretpostavljamo da se ovde radi o novom tumorskom markeru. Međutim, dalja istraživanja su neophodna da se dokaže da je BG–9 antigen novi tumor–specifični marker.

**Zaključak** – U okviru ovog rada imunohistohemijski je okarakterisano mišje monoklonsko antitelo BG-9 protiv Novog Prostata-Specifičnog Antigena koje delimično ukršteno reaguje sa tkivima malignog melanoma. Utvrđeno je da ovaj antigen ne podleže denaturaciji u prisustvu fiksacionih agenasa kao što su formalin, aceton ili etanol, čime se otvara mogućnost za retroaktivna histopatološka ispitivanja.

Naši dosadašnji rezultati ukazuju da BG-9 antigen može da se upotrebi slično kao PSA i PSAP, u dijagnostici tumora prostate. Za razliku od prethodnih, BG-9 antigen je lokalizovan i na ćelijama epitela izvodnih kanalića benigne hiperplazije prostate čime se otvaraju nove mogućnosti u dijagnostici tumora prostate.

**Napomena** – Zahvaljujemo se svim kolegama iz Instituta za patologiju, VMA u Beogradu kao i kolegama iz Instituta za onkologiju iz Beograda i Sremske Kamenice na saradnji i podršci u ovom radu. Takođe želimo da naglasimo požrtvovanu tehničku pomoć Saše Vojnova i Emilije Nestorović u dobijanju i održavanju monoklonskog antitela BG-9 u Vinči. Ovo istraživanje finansira Fond za nauku SR Srbije.

**Sažetak**

Cilj ovog rada je procena primenjivosti monoklonskog antitela BG-9 u dijagnostici tumora prostate pomoću imunohistohemijske PAP tehnike kao prihvaćene predkliničke metode za određivanje specifičnosti monoklonskih antitela. Ispitano je ukupno 188 postoperativnih humanih tkiva ili biopsija koji su obuhvatili sveže ili formalinom fiksirane isečke. Pozitivno imunohistohemijsko bojenje je dobijeno na ćelijama epitela izvodnih kanalića i žljezdanih struktura u 54/59 slučaja benigne hiperplazije prostate kao i na žljezdanim strukturama u 22/22 slučaja karcinoma prostate. Zastupljenost BG-9 antigena je dokazana i na malignim melanocitima u 9/24 slučaja malignog melanoma. Ostali uzorci tkiva, uključujući 30 isečaka drugih maligniteta, 8 benignih isečaka, 21 zdravu prostatu i 24 ostala zdrava tkiva, nisu reagovali sa BG-9. Naši dosadašnji rezultati ukazuju da je monoklonsko antitelo BG-9 specifično za tumor prostate i ukršteno reaktivno sa tkivima malignog melanoma. Time se BG-9 antigen klasifikuje, slično kao PSA ili PSAP, u grupu prostata-specifičnih antigena. Za razliku od prethodnih, BG-9 antigen je zastupljen na ćelijama epitela izvodnih kanalića i potencijalan imunohistološki marker za karcinome izvodnih kanalića prostate. Pomoću ovakvog markera je moguće razlikovati slabo diferentovani adenokarcinom prostate od nediferentovanog karcinoma izvodnih kanalića prostate. Time se otvaraju značajne dijagnostičke i terapeutske mogućnosti za primenu monoklonskog antitela BG-9 u kliničkoj praksi.

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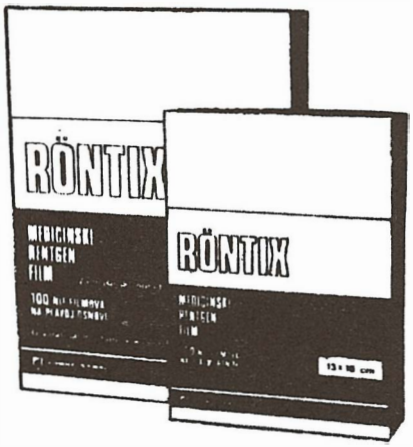
# RÖNTIX

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# DIAGNOSIS AND TREATMENT WITH PERCUTANEOUS CATHETER DRAINAGE UNDER ECHOGRAPHIC CONTROL OF A SUBPHRENIC ABSCESS – CASE REPORT

Čengić-Huković F, Čengić F, Bajgorić M

**Abstract** – Bacterial hepatic abscesses are a rare but serious disease. The diagnosis is confirmed by ultrasonography and by aspiration under ultrasonographic guidance. The therapy consists of administration of antibiotics and percutaneous drainage.
Sonographically guided fine-needle aspiration and percutaneous drainage is a simple and effective procedure for the treatment of subphrenic abscess and should be considered as an alternative to surgery.

**UDC:** 616.36-002.3-089.48

**Key words:** liver abscess, ultrasonic diagnosis, drainage

**Letter to the Editor**

**Radiol Iugosl** 1991 ; 25 : 69-70

**Introduction** – Bacterial hepatic, subphrenic, subhepatic abscesses are formed because of injuries or ischemia, infection of the drainage area of the portal vein, systemic sepsis and biliary infections. US is superior to CT for subphrenic and subhepatic areas specially for collections adjacent to the abdominal wall; CT is superior to US for retroperitoneal deeply localised or »unsatisfactory« US fluid collection. Low cost of US, the possibility of very frequent checks without risk or radiation, wide availability, and multiplanar imaging, are some additional advantages comparing to other tchniques.

**Case Report** – A 69-years old male had become febrile three days before hospitalised with clinically suspected intraabdominal abscess (profuse sweats, leukocytosis, weakness, nausea, vomiting). Echographic scanning (axial, coronal, sagittal) presented a large subphrenic abscess 8x4 cm, uniloculated, cloudy as well as cholangitis and cholecystitis calculosa. Percutaneous aspiration was performed with 20 G needle: the material was sent for microbiological, cytological, chemical and haematological analyses. The abscess was drained by US-guided Seldinger technique (Sal 77 Toshiba 3,75 MHz) and irrigated by saline lavages twice a day for the first 5 days, and once a day for the next 7 days via 9 French pig tail catheter and antibiotics (gentamycin 2 mg). The patient became afebrile within $24^{h}$ after drainage, partial resolution of abscess was observed 7 to 10 days later. The duration of drainage was 12 days and the patient recovered without surgery. On the follow-up check month later we established a good restitutio ad integrum.

**Discussion** – Despite the continuous advances in diagnostic imaging and treatment, hepatic abscess remains a serious clinical problem. Sonographically guided fine-needle puncture and percutaneous drainage is a simple and effective procedure for the treatment of subphrenic abscess or fluid collections localized adjacent to the abdominal wall. Real time sonographic imaging should be considered as an alternative procedure to surgery. . .

**Conclusions** – In our case, US guided percutaneous drainage was performed as a diagnostic and therapeutic method. The presented compared with literature, indicated that percutaneous catheter drainage in combination with antibiotics can be the definitive therapy.

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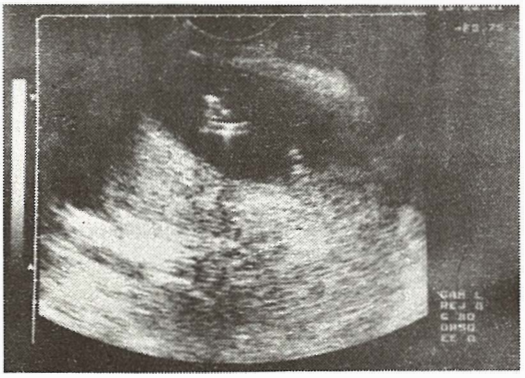

Fig. 1 – Abscess – catheter in place

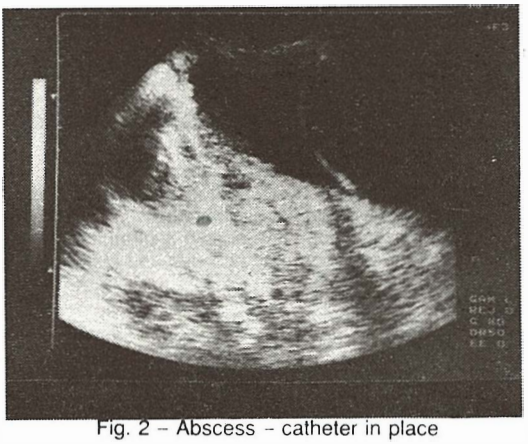

Fig. 2 – Abscess – catheter in place

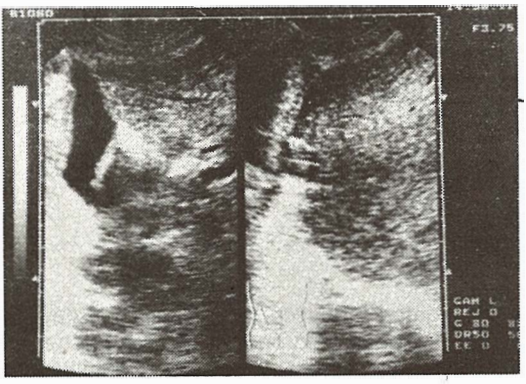

Fig. 3 – Partial resolution of abscess 7 and 10 days after catheter placement (arrows)

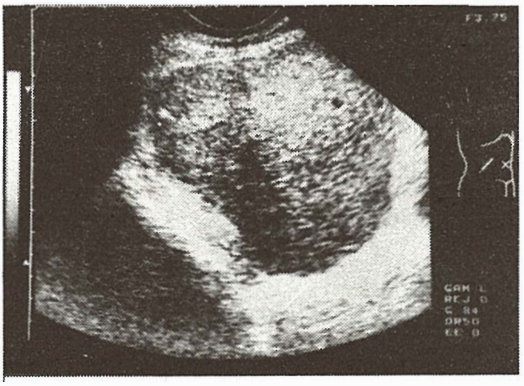

Fig. 4 – Follow-up check a month later

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# BURKITT – LIKE LYMPHOMA IN CENTRAL EUROPE

**October 18 – 19th, 1990**
**Ljubljana**

Symposium on Burkitt – like lymphoma in Central Europe was held in Ljubljana on October 18th and 19th 1990, in a large part thanks to Mercator trade company, that generously provided its conference facilities. It was held under the auspices of European School of Oncology from Milan, and organized by Chair of Oncology, Medical faculty, University of Ljubljana, and the Institute of Oncology, Ljubljana. The aim of organizing commitee was to bring together as many experts that deal with this disease as possible, since Burkitt – like lymphoma is not frequently diagnosed outside Africa. It is nevertheless occasionally encountered in clinical practice all over Europe and North America, but since the number of cases collected even over longer periods of time and in large centers rarely exceeds two – digit numbers, it is rarely possible to produce a larger series of patients. A critical analysis of collected data, so was assumed, could help the participants to outline the most effective treatment methods.

The symposium was roughly divided in two parts. On the first day a special lecture, considering the present status of the role of immunotherapy in the treatment of malignancies, was given by M. J. Mastrangello (Jefferson Univesity, Philadelphia), followed by the lectures considering epidemiology and virology of Burkitt – like lymphoma, given by M. Coleman (IARC, Lyon), pathology and immunology of Burkitt – like lymphoma, given by A. Carbonne (Oncology Referal Centre, Aviano), and about symptomatology and staging of Burkitt – like lymphoma, given by M. Gasparini (National Tumour Institute, Milan).

On the next day a lecture on the present status of treatment of Burkitt – like lymphoma was given by R. Kath (West German Tumour Centre, Essen), and was followed by poster presentations and short lectures considering the characteristics of Burkitt – like lymphoma and its treatment. They were given by participating experts coming from Milan, Belgrade, Trieste, Warsaw, Zagreb, Bratislava, Essen, Aviano and Ljubljana. During this session, chaired by S. Monfardini (Oncology Referal Centre, Aviano), various modalities of treatment of 166 patients with this disease, used in the oncology centres mentioned above, were presented. The number of Burkitt – like lymphoma patients presented is probably one of the largest collected so far. Some interesting observations were pointed out by some of the participants in this discussion. S. Jelić et al. (Institute of Oncology and Radiology, Belgrade) found out, that the majority of their patients lived close to the rivers in the river basin of Danube, while U. Tirelli et al. (Oncology Referal Centre, Aviano) reported an increased incidence of this disease in patients with HIV infection. Cure rates ranged from 20-100% and all of the participants agreed, that an intensive combination chemotherapy treatment should be started immediatelly after the diagnosis of Burkitt – like lymphoma has been confirmed. On the other hand, U. Tirelli et al. reported that patients with concomitant HIV infection and Burkitt – like lymphoma have a significantly lower median age and poorer prognosis, and H. Minigo et al. (Clinical Hospital Dr. O. Novosel, Zagreb) reported long term complete remissions in three out of five patients, treated by Cyclophosphamide monotherapy. At the end of the discussion the chairman suggested that a monograph on this disease should be published and a treatment protocol developed to be used by all interested participants and others.

In the opinion of all the participants the symposium was quite succesfull and all members of organizing commitee hope that this one was only the first of many Rare Tumours Symposia that should be held in Ljubljana under the auspices of European School of Oncology. Malignant melanoma during pregnancy, T – cell lymphoma, Sezary syndrome, Lymphoma associated with HIV infection and Carcinoid are among the topics suggested.

Andrej Plesničar, M. D.

## RENTGENOLOGIJA – DIAGNOSTIČNE SLIKOVNE METODE IN INTERVENCIJSKA RADIOLOGIJA

Knjiga je razširjena in izpolnjena izdaja učbenika RENTGENOLOGIJA – DIAGNOSTIČNE SLIKOVNE METODE iz leta 1984. Večje število avtorjev in soavtorjev se je dela lotilo kompleksneje in bolj ambiciozno. Učbenik je razdeljen v dva dela, splošni in posebni del in zajema v celoti 23 poglavij.

Splošni del obravnava lastnosti rentgenskih žarkov, ki se uporabljajo v medicini, osnove rentgenske tehnike, splošna načela čitanja in razlage rentgenogramov, kot tudi zaščito bolnikov in radioloških delavcev pred ionizirajočim sevanjem pri rentgenski diagnostiki in terapiji. Temu delu so dodane osnovne smernice novejših metod, ki jih dandanes v glavnem obvladuje rentgenologija, kot so kseroradiografija, računalniška tomografija in magnetna resonanca. Pomemben je opis kontrastnih sredstev, ki se uporabljajo v radiologiji, kot tudi opis možnih odzivov organizma na kontrastna sredstva, njihovo preprečevanje in zdravljenje. V kratkih črtah je dodan diagnostični ultrazvok, ki ne spada direktno k radiologiji, vendar didaktično smiselno zaokroža paleto diagnostičnih metod. Na koncu splošnega dela je pomembno poglavje o intervencijski radiologiji, metodi, ki združuje diagnostičen postopek s terapevtskim in postaja v zadnjem času vse bolj pomembna pri zdravljenju najrazličnejših bolezni.

Posebni del obravnava organe in organske sisteme, možnosti sodobnih radioloških diagnostičnih metod in njihovo zmogljivost v diagnostičnem postopku. Opisani so prsni organi, posebej srce in posebej kontrastne preiskave srca in žil, pa trebuh, prebavila, jetra in vranica, žolčnik, žolčni vodi in trebušna slinovka, sečila, okostje in gibala, posebej lobanja, osrednje živčevje, radiološke preiskave rodil in mehkih delov. Ponavadi je na začektu vsakega poglavja prikazana normalna rentgenska anatomija, dočim so patološka dogajanja oziroma entitete osvetljene nekje manj drugje bolj s patološko anatomskimi, fiziološkimi in predvsem kliničnimi opisi. Vselej je podrobneje opisana radiološka slika posamezne bolezni. Ta sinteza daje učbeniku večjo vrednost in širšo uporabnost ter predstavlja sodobno radiologijo kot izrazito interdisciplinarno vedo.

V nekaterih poglavjih so dodatno opisane metode intervencijske radiologije, tako da se nekateri opisi ponavljajo, vendar ne toliko, da bi to učbeniku škodilo. Vsa poglavja v posebnem delu so bogato ilustrirana s shemami, slikami rentgenogramov, računalniške tomografije, ultra-zvoka in magnetne resonance. Gre za preko 500 slik, ki povečujejo vrednost knjige in ponazarjajo skokovit razvoj novih radioloških tehnologij.

Knjiga je napisana kot sodoben učbenik z dovolj sistematičnim in pedagoškim pristopom. Odlikuje jo, v večjem delu, klinična razlaga radioloških sprememb in postopkov, zato jo priporočam študentom medicine, specializantom kliničnih vej medicine in drugim zdravnikom.

prof. dr. Miran Kenda

## Radiologie II
## Lehrbuch für den 2. Abschnitt der Ärztlichen Prüfung, das Praktiche Jahr und die Fachärztliche Weiterbildung

Herausgegeben von Prof. Dr med., Dr. h. c. **J. LISSNER,** Direktor der Radiologischen Klinik und Poliklinik im Klinikum Großhadern der Univ. München, und Priv.-Doz. Dr. med. **U. FINK,** Akademischer Rat, Oberarzt der Radiologischen Klinik im Klinikum Großhadern, München

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Die 3., völlig neu gestaltete Auflage des bewährten Lehrbuches gibt einen Überblick über das gesamte Geibet der klinischen Radiologie. Die drei Fachgebiete Radiologische Diagnostik, Nuklearmedizin und Strahlentherapie werden in gesonderten Kapiteln mit zahlreichen, zum größten Teil neuen Abbildungen abgehandelt. Neben den eingeführten bildgebenden Verfahren werden zu jedem Organsystem die Einsatzmöglichkeiten und der klinische Stellenwert neuster radiologischer Verfahren wie zi. B. der Kernspintomographie, der Single-Photon-Emmissionscomputertomographie (SPECT) und der intraoperativen Strahlentherapie besprochen.

**Interessenten:**
**Studenten der Humanmedizin.**

Arzte im Praktikum, Ärzte in Weiterbildung speziell für Radiologische Diagnostik, Strahlentherapie und Nuklearmedizin, Teilgebietsradiologen.

**Inhaltsübersicht:**

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## MAGNETRESONNANZTOMOGRAPHIE BEI ASEPTICHER OSTEONEKROSE DES FEMURKOPFES

### Möglichkeiten der Frühdiagnosik – Histologische Korrelation – Dreidimensionale Rekonstruktion

Von Dr. med. **P. LANG,** Hochschulassistent, Department of Radiology der University of California, San Francisco

1990. XX, 148 Seiten, 54 Abbildunge, 32 Tabellen, 14,8 x 21 cm, < Copythek > ca. DM 45,-
ISBN 3 432 80211 0

Die Hüftkopfnekrose ist eine zunehmend häufiger zu verzeichnende Erkrankung, die sowohl Orthopäden und Radiologen als auch Rheumatologen und Allgemeinmediziner vor schwerwiegende diagnostische und therapeutische Probleme stellt. Das vorligende Buch vermittelt einen detaillierten Überblick über die Symptomatik, den Verlauf, die Ätiologie und Pathogenese sowie die Diasgnostik und die Therapie der Hüftkopfnekrose. Besondere Aufmerksamkeit wird dem jüngsten und in vieler Hinsicht am meisten versprechenden bildgebenden Verfahren zum Nachweis der Hüftkopfnekrose, der Magnetresonanztomographie, gewidmet. Die Prinzipien der Magnetresonanztomographie werden in kurzer, allgemein verständlicher Form beschrieben. Jüngste Forschungsergebnisse, wie die Diagnostik des akuten ischämischen Insultes des Knochenmarkes, die Bestimmung des histomorphologischen Stadiums der Nekrose mit der Magnetresonanzitomographie sowie die dreidimensionale Bildgebung zur Operationsplanung, werden umfassend abgehandelt.

**Inhaltsübersicht:**

*Einleitung* Die Magnetrosonanztomographie– ein modernes bildgebendes Verfahren Aseptische Osteonekrose des Femurkopfes Ziele der geienem Untersuchungen *Möglichkeiten der Frühdiagnostik der MRT bei akut induzierter Ischämie und Osteonekrose des Schweinefemurkopfes Korrelation von MRT-Bildbefunden mit histologischen Großflächenschnitten Dreidimensionale Rekonstruktion.*

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## PROF.DR. GOJMIR KLANJŠČEK

Bil je vedno poln sile, inzajdljiv in pronicljiv ter nepredvidljiv. In tako nas je tudi zapustil. Nihče ni predvideval, da ga nenadoma ne bo več med nami, saj je bil poln zdravja in še poln moči. Odšel je povsem nepričakovano, v času, ko je bilo še toliko storiti in ustvarjalno pregledati.

Dr. Gojko Klanjšček, neprekosljiv diagnostični radiolog, odličen prijatelj, do skrajnosti natančen pri svojem iskanju in raziskovanju, nas je zapustil leta 1990, v 70.letu starosti.

Na kratko o njegovem življenju. Rodil se je v Rogaški Slatini; pred vojno se je vpisal na Medicinsko fakulteto v Zagrebu, ki jo je zaključil v Padovi. Specijalizacijo iz rentgenologije je opravil v takrat odlični rentgenski šoli na Vojno–medicinski akademiji v Beogradu, specialistični izpit pa opravil leta 1951. Nato je delal kot rentgenolog v Vojaški bolnici v Ljubljani, kjer je dalj časa opravljal dolžnosti šefa tega oddelka. Leta 1965 se je redno zaposlil na Onkološkem inštitutu v Ljubljani, kjer je vršil naloge vodje enote za rentgensko diagnostiko. Primarij je postal leta 1967, doktorat znanosti pa je dosegal leta 1973; kasneje je dobil naslov nazivnega profesorja rentgenologije. Kot visoko razgledan strokovnjak je bil profesor Klanjšček tudi sicer aktiven, saj je sodeloval s svojimi prispevki v številnih nacionalnih in mednarodnih kongresih, v nizu raziskoralnih nalog Onkološkega inštituta in s tem v zvezi objavil številna strokovno–znanstvena dela v domači in tuji literaturi. Zelo aktiven je bil tudi na pedagoškem področju, saj je z zavzetostjo poučeval specializante, ki so pri njem redno gostovali in sprejemali njegovo bogato in temeljito znanje onkološke rentgenidiagnostike. Nadalje je sodeloval pri pouku slušateljev petega letnika Medicinske fakultete ter s tem v zvezi tudi zasnoval in izdelal nekatere raziskovalne naloge, pri katerih so sodelovali slušatelji petega letnika Medicinske fakultete v Ljubljani. Bil je aktivan član Mednarodnega združenja za limfologijo. Pri vsem tem pa je vedno pazil, da je obdržal svojo visoko strokovno raven s stalnim izpopolnjevanjem, saj je sodeloval in se udeleževal številnih sodobnih tečejev, kongresov, znanstvenih sestankov, okroglih miz in delavnic doma, predvsem pa v tujini. Tudi po upokojitvi je bil aktiven in je z drugimi zdravniki sodeloval pri ugotovljanju patologije kosti pri izkopanih skeletih starih Slovanov na področju Kranja. Uredniki našega časopisa se ga spominjamo kot zvestega sodelavca, ki nam je skozi leta vztrajno pomagal, bodisi kot avtor bodisi pri raznih prepotrebnih strokovnih ocenah in mnenjih ter recenzijah prispevkov.

S smrtjo prof. Klanjščka se zaključuje določeno obdobje razvoja rentgenske diagnostike na Onkološkem inštitutu v Ljubljani. Od enega samega skromnega rentgenskega aparata ob njegovem prihodu na Inštitut, imamo danes, kot plod njegove nenehne in takorekoč trmaste ustvarjalnosti, sodoben oddelek, ki s svojo kvaliteto dela v celoti zadošča zahtevam moderne onkologije. V njegovem času je bila vpeljana mamografija, limfografija in začelo se je z ultrazvokom. Ob teh novih dejavnostih pa so se do odličnosti razvile ostale že obstoječe diagnostične dejavnosti, pomembne za onkologijo, kot so diagnostika kostnega sistema, pulmonalna diagnostika in druge. Nikakor ni prezreti tega, da je v daljnjem letu 1965 delal v rentgenski diagnostiki sam, samcat, in da je kot plod svojega dela vzgojil skupino mladih specialistov, ki sedaj opravljajo svoje delo učinkovito in dobro kot verni nasledniki raziskovalne in strokovne zapuščine pokojnega profesorja.

Ohranili ga bomo v najboljšem spominu, kot radiologa ostrega uma, neprekosljivega diagnostika in trdega ter predanega delavca. Ohranili bomo spomin nanj, kot na dobrega prijatelja in sodelavca. Spomin na človeka, ki nikoli ni odklonil pomoči, če je bilo treba pomagati bodisi bolniku bodisi svojemu kolegu. Imeli smo radi človeka, ki je bil prijeten, čeprav strog in neizprosen učitelj mladih zdravnikov, a hkrati tudi spoštljiv do svojih starejših kolegov. Njegova družabnost je bila naravnost pravljična. S svojim dražečim humorjem je znal vcepiti ljudem neko živahnost in veselost, ki je bila v družbi z njim naravnost nalezljiva. Bil je dejansko osišče, okoli katerega se je sukalo življenje in veselje do življenja.

Na koncu moramo reči, da je odšel prezgodaj, vendar ne bomo rekli, da je zapustil za seboj vrzel, ki se je ne da zapolniti. Nobene vrzeli ni za njim, kajti poskrbel je, da tudi po njegovem odhodu potekata delo in razvoj v njegovi stroki naprej, brez prestanka in zastoja. V tem je ravno ta velika vrednost ustvarjalca. In kot takega ga bomo ohranili v spominu, kot človeka in osebnost, ki je v svojem času, v trdih in neizprosnih povojnih letih, pustil svoj neizbrisni pečat kreativnosti.

**Prof. dr. Stojan Plesničar**

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# AUTHOR'S INDEX 1990





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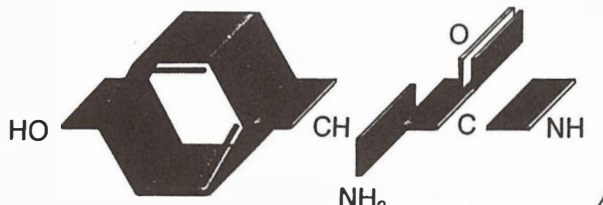


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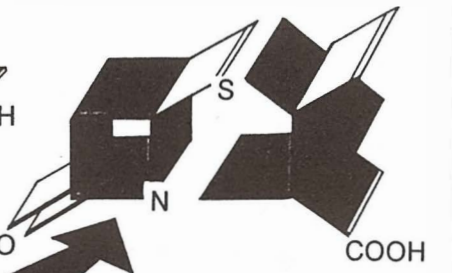


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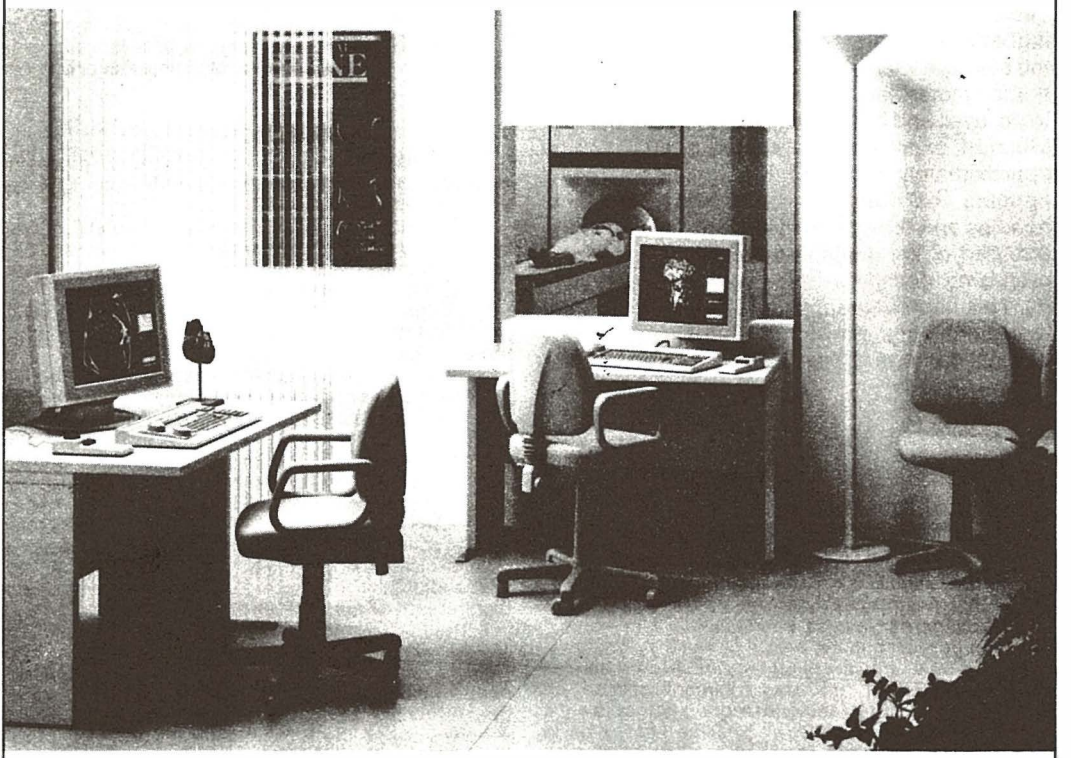

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1. Ďent RG, Cole P. In vitro maturation of monocytes in squamous carcinoma of the lung. Br J Cancer 1981; 43:486–95.
2. Chapman S, Nakielny R. A guide to radiological procedures. London: Bailliere Tindall, 1986.
3. Evans R, Alexander P. Mechanisms of extracellular kiling of nucleated mammalian cells by macrophages. In: Nelson DS ed. Immunobiology of macrophage. New York: Academic Press, 1976; 45–74.

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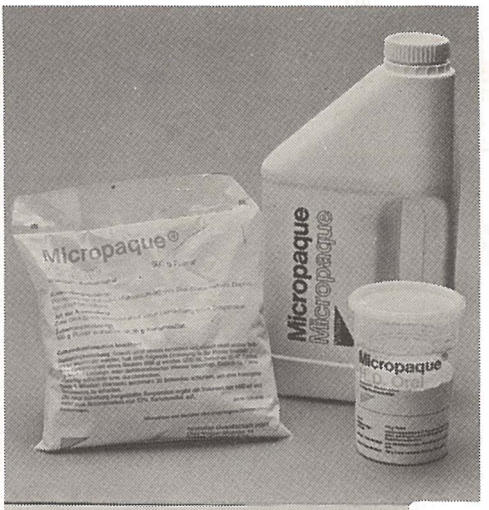


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**Micropaque® suspenzija**
**Micropaque® Colon**

**Nicholas**

KEMIKALIJE ZA STROJNU I RUČNU OBRADU MEDICINSKIH FOTOMATERIJALA

Efke EKG papir: -001
-002
-003

POLAROID: -crno-bijeli 667
-kolor 339

**FOTOKEMIKA**

**Poduzeće za proizvodnju i promet fotografskih materijala i opreme s p.o. ZAGREB, Hondlova 2, TEL. 041/231-833, Telex: 22-214 YU FOKEM, Telefax: 041/232-653**

PHILIPS

avtotehna

PHILIPS

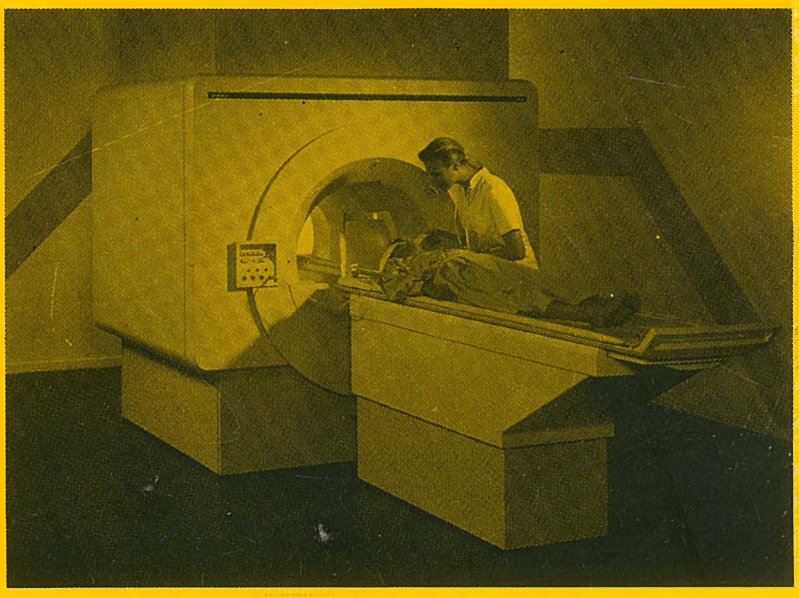
Philips Medical Systems

# *Gyroscan T5*

## Revolucija v MR diagnostiki

Philips je v prvem letu po predstavitvi Gyroscana T5 (0,5T) prodal že več kot 120 aparatov.
Naše stranke se odločajo za T5 zaradi:

- izredne kvalitete slike, ki je praktično enakovredna slikam 2T magnetov;
- majhnih prostorskih zahtev (5 x 7 m);
- zaradi aktivne zaščite ne potrebuje dodatne zaščite in posebnih stavb;
- enostavno in hitro delo;
- enostavno vzdrževanje
- in ne nazadnje zaradi cene, ki se je že približala ceni CT-ja



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