The Value of Duplex ultrasound versus contrast enhanced CT Scan in the follow-up of Endoluminally repaired Abdominal Aortic Aneurysm: A blinded study

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ABSTRACT

The value of duplex ultrasound versus contrast enhanced CT scan in follow-up of patients with endoluminally repaired aortic aneurysms: a blinded comparison.

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Objectives

1-To compare aneurysm diameter measurements, and the detection of endoleaks in patients post endoluminal aortic aneurysm repair by colour duplex ultrasonography as compared to contrast enhanced CT scan as the gold standard.

2-To evaluate whether contrast enhanced ultrasound (levovist) improves the accuracy of colour duplex ultrasound for the detection of endoleaks as compared to CT.

Methods

Fifty one patients with endoluminal repair of abdominal aortic aneurysm were evaluated concurrently with both contrast enhanced CT and duplex ultrasonography at two university hospitals. By the end of the study period 89 exams results were available for diameter measurements and 86 for endoleak detection and made up the study sample. In addition, one hospital provided 38 contrast enhanced (levovist) duplex exams. Anteroposterior (AP) and transverse (T) aneurysm diameters were compared between CT and duplex ultrasound. The presence and type, or absence of endoleak was also defined by both modalities. Radiologists performing the duplex scans were blinded with respect to the CT result.

Results

Diameter measurements were consistently larger by CT [mean (SD) CT - duplex AP diameter difference (cm) = 0.25 (0.34) cm, p=0.001]. Changes in aneurysm Diameters between serial scans were comparable between CT and duplex.

Table 1:Detection of endoleaks

	CT results		
US results	leak	no	Total
leak	13	8	21
No	13	52	65
Total	26	60	86

Sensitivity = (13/26)× 100=50%

Specificity = (52/60)× 100=86.7%

Positive predictive value =(13/21)× 100=61.9%

Negative predictive value =(52/65)× 100=82%

Kappa coefficient (95% Confidence Interval) 0.4 (0.2-0.6) ($p<0.05$)

Three out of 13 false negative endoleaks by duplex were found in aneurysms that had increased in size when compared to the preoperative CT. The detection of endoleaks by duplex was not significantly influenced by patient characteristics such as obesity, nor by the quality of the exam and the addition of ultrasound contrast.

Conclusions

Duplex ultrasonography had comparable accuracy with CT for evaluation of aneurysm diameter post endoluminal repair. There was only moderate agreement between duplex and CT for detection of endoleaks. CT was more reliable for detecting endoleaks associated with aneurysm growth. Contrast enhanced duplex did not change the accuracy of duplex ultrasonography for detection of endoleaks.

Résumé

La valeur de l'échographie duplex comparée à celle du CT scan avec injection de contraste lors du suivi des patients ayant subi un traitement endovasculaire pour un anévrisme de l'aorte abdominale.

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Objectifs

1) Mesurer le diamètre des anévrismes ainsi que détecter les endofuites chez les patients traités de façon endovasculaire pour un anévrisme de l'aorte abdominale, en comparant les résultats de l'échographie duplex en couleurs à ceux du CT scan avec injection de contraste, ce dernier étant considéré comme l'examen de référence.

2) Evaluer si l'échographie duplex avec injection de contraste (levovist) améliore la précision de l'échographie duplex en couleurs pour la détection des endofuites, comparativement au CT scan.

Méthode

Cinquante-et-un patients ayant subi un traitement endovasculaire pour anévrisme de l'aorte abdominale ont été évalués à la fois par CT scan avec injection de contraste et par échographie duplex, dans deux hôpitaux universitaires. À la fin de la période, il y avait donc 86 examens disponibles pour l'étude des diamètres anévrismaux ainsi que des

endofuites, ce qui correspond à la cohorte étudiée. De plus, dans l'un des centres universitaires, 28 patients ont eu un total de 38 examens duplex avec injection de contraste (levovist). Les résultats des diamètres transverses et antéro-postérieurs obtenus par CT scan et par échographie duplex ont été comparés. La présence et le type, ou encore l'absence d'endofuites ont également été évalués de façon concomitante à l'aide des deux modalités radiologiques. Les radiologistes effectuant les échographies duplex ne connaissaient pas les résultats des CT scan.

Résultats

Les diamètres évalués par CT scan étaient significativement plus grands que ceux par duplex (différence moyenne du diamètre antéro-postérieur entre CT scan et duplex = 0,25 cm +/- DS 0,34 cm, p=0,001). Les changements de diamètre anévrismal entre examens consécutifs étaient comparables entre le CT scan et l'échographie duplex.

Tableau 1 : Détection des endofuites

	Résultats CT scan		
Résultats échographie	Endofuites +	Endofuites -	Total
Endofuites +	13	8	21
Endofuites -	13	52	65
Total	26	60	86

Sensibilité = (13/26) X 100 = 50%
Spécificité = (52/60) X 100 = 86,7%
Valeur prédictive positive = (13/21) X 100 = 61,9%
Valeur prédictive négative = (52/65) X 100 = 82%
Coefficient kappa (95% intervalle de confiance) 0.4 (0.2-0.6) $p<0.05$

Il y a eu 13 faux-négatifs dans la détection des endofuites par Duplex. Trois de celles-ci provenaient d'anévrismes dont la taille avait augmenté comparativement au CT scan préopératoire. La détection des endofuites par Duplex n'était pas influencée de façon significative par les caractéristiques du patient telle que l'obésité, ni par la qualité de l'examen ou l'addition de l'échographie avec injection de contraste (levovist).

Conclusions

À la suite d'un traitement endovasculaire pour anévrisme de l'aorte abdominale, l'échographie duplex a une précision comparable au CT scan en regard à la mesure du diamètre anévrismal. Seule une corrélation modérée a été observée entre le Duplex et le CT scan en ce qui a trait à la détection des endofuites. Par ailleurs, le CT scan était plus fiable pour déceler les endofuites associées à une croissance anévrismale. L'identification des endofuites détectées par l'échographie duplex n'a pas été plus précise avec l'ajout de l'échographie duplex avec injection de contraste.

ABBREVIATION INDEX

AAA : Abdominal Aortic Aneurysm.

AP : Antero-Posterior.

cc : Cubic Centimeter.

CECT : Contrast Enhanced Computed Tomography.

cm : Centimeter.

CT : Computed Tomography.

CTA : CT Angiography.

DUS : Duplex Ultrasound.

EL : Endoleak.

FU : Follow up.

IVUS : Intravenous Ultrasound.

MHz : Mega Hertz.

mm : Millimeter.

MRA : Magnetic Resonance Angiography.

3-D : Three Dimensional.

T : Transverse.

U/S : Ultrasound.

BACKGROUND

Abdominal aortic aneurysms (AAA) are a common problem in developed countries and represent a significant public health risk. Operative repair is the only acceptable method to reduce the risk for rupture and the associated mortality, and the treatment algorithm represents a balance between the estimated risk of operation and the future risk for rupture. The standard operative technique has been refined during the past five decades since the first successful aneurysm resection in 1951 by Dubost et al (34).

Definitions and classifications

An aneurysm is defined as a permanent, focal dilatation of an artery in which the diameter is increased to 1.5 times the normal expected diameter (33). The dimeter of a normal abdominal aorta in a male adult is approximately 2 cm (range 1.4-3 cm) (35), and therefore a 3 cm aorta would be considered aneurysmal.

Abdominal aortic aneurysms are classified primarily according to how far they extend proximally. More than 95% of all abdominal aortic aneurysms are classified as infrarenal (36). These aneurysms start below the takeoff of the orifices of the renal arteries and usually have a 1.5-2.0 cm normal infrarenal aortic cuff. Aneurysms classified as juxtarenal extend proximally to the level of the renal arteries, and those classified as suprarenal extend proximally to the level of the superior mesenteric and/or celiac arteries. Aneurysms involving the thoracic and abdominal aorta are classified (types 1 through 4) according to how far they extend proximally and distally.

Magnitude of the problem

Abdominal aortic aneurysm and their sequelae are common problems in developed countries. The incidence of AAA in the United States ranges from 1.5% in autopsy series to 3.2% among unselected adult patients screened with ultrasonography (36). Predictably, the incidence increases among subsets of patients with defined risk factors for AAA and approximately 50% among patients with either femoral or popliteal aneurysms (36). Approximately 8,700 deaths caused by AAA were reported by the National Centre for Health Statistics in 1990 (37). These figures correspond to an incidence of death of 0.8% among men and 0.3% among women. The numbers are likely underestimates because a significant number of sudden deaths in elderly patients may be secondary to undiagnosed ruptured aneurysms.

Pathogenesis and Risk factors

The pathogenesis of AAA remains unresolved, although it has been an intense area of both experimental and clinical investigation. Multiple potential etiologic factors have been implicated, including atherosclerotic degeneration (38), hemodynamic changes (39), disorders of collagen (40), and collagenase (41), disorders of elastin (42), and elastase (43), abnormalities of metalloproteinases (44), and protease inhibitors (45), programmed cell death (apoptosis) (46), and inflammatory mediators (47). Unfortunately, investigation into the potential mechanisms has not resulted in new theraputic strategies. Elucidation of the pathogenesis has been complicated by the advanced age of patients at presentation and the absence of suitable animal models. Multiple risk factors have been identified for the development of abdominal aortic aneurysms and include age, sex, smoking history, hypertension, hyperlipidemia, and family history (48). Identification of these risk factors is important to facilitate screening high-risk patient population and potentially initiating treatment earlier.

Principles of management

The treatment goals for patients with AAA are to prolong life, relieve symptoms, and prevent rupture. Because surgical treatment is the only effective means to achieve these goals, the crucial question that should be answered is whether the patient must undergo an operative repair. The decision algorithm is straight forward for patients with ruptured or symptomatic aneurysms, but more difficult for patient with asymptomatic, intact aneurysms. The decision to recommend an operative intervention in the elective setting is contingent on the balance between the risk of operation and the risk of expectant or non-operative management. The risk for rupture of an AAA is related to its diameter, as would be predicted by the tangential stress of the vessel wall. A recent collective review reported the annual rupture risk to be 4.1% for aneurysms 5 cm in diameter, 6.6% for those between 5 to 7 cm in diameter, and 19% for those 7 cm in diameter (36). The natural history of abdominal aortic aneurysm is an increase in diameter with time. An estimated 80% of all small aneurysms continue to grow (33). The mortality rate associated with repair of an AAA primarily depends on the status (intact/asymptomatic, intact/symptomatic, ruptured) of the aneurysm. A recent study reported the mortality rate in more than 15,000 repairs of intact AAA in the united states to be 4.2% (49). Predictably, the operative mortality risk increased with age, ranging from 2.2% among persons 50 to 59 years old to 9.2% among those older than 80 years. Interestingly, the operative mortality was higher among women (6.1% versus 3.7%). The actual mortality rate for ruptured AAA is somewhat difficult to determine because a significant number of sudden deaths in elderly patients are likely secondary to ruptured aneurysms. It has been estimated that 50% of all patients with ruptured AAA die before reaching the hospital, and that approximately 50% of those who actually undergo surgery die (36). These figures correspond to an overall mortality rate of approximately 80%, although this may be an underestimate.

Brief description of the open (standard) technique for repair of abdominal aortic aneurysm (55)

When using the transperitoneal approach, the small bowel is mobilized to the right and the posterior peritoneum overlying the aortic aneurysm is divided to the left of the midline . The duodenum is mobilized and the left renal vein is identified and exposed. The nonaneurysmal infrarenal neck, immediately below the left renal vein is exposed and encircled to obtain proximal control. The common iliac arteries are then mobilized and controlled, taking care to avoid the underlying iliac veins and ureters that cross over the iliac bifurcation. If the common iliac arteries are aneurysmal, control of the internal and external iliac arteries is obtained. The inferior mesenteric artery arising from the anterior aspect of the aneurysm is exposed and controlled for possible reimplantation into the graft after aneurysm repair. After systemic anticoagulation with intravenous heparin, the infrarenal aorta and iliac arteries are cross-clamped. The aneurysm is opened longitudinally; mural thrombus is removed and backbleeding lumbar arteries are oversewn. Depending on its backflow and on patency of hypogastric arteries, the inferior mesenteric artery may be ligated or clamped and left with a rim of aortic wall for subsequent reimplantation. The aneurysm neck is partially or completely transected and an appropriately sized tubular or bifurcated prosthetic graft is sutured to the normal infrarenal aorta with monofilament permanent nonabsorbable suture. In the case of juxtarenal aneurysms in which there is a very short or absent neck, suprarenal aortic clamping may be necessary to perform the proximal anastomosis. The distal graft anastomosis is performed to the aortic bifurcation when the aneurysm is confined to the aorta. This is known as "tube graft" reconstruction. Tube grafts are used in 30 to 50% of patients. Patients with iliac aneurysms are reconstructed with bifurcated grafts anastomosed to the distal common iliac arteries or to the common femoral arteries in the case of significant associated external iliac disease. The open aneurysm sac is sutured closed over the aortic graft to separate the graft from the duodenum and viscera, preventing the possibility of late aorto-enteric fistula formation.

Brief description of the endovascular technique for repair of abdominal aortic aneurysm (55)

The technical details of endovascular repair vary with each specific device but the general principles are similar. In most cases, a self-expanding stent graft is inserted into the aorta by way of the femoral arteries. At the present time, the insertion requires surgical exposure of both common femoral arteries. The arteries are cannulated and guide wires are inserted into the aorta. Most stent grafts are made of two pieces: a main module including the body and one of the limbs with a gate for the separate contralateral limb. The appropriately sized primary module is inserted under fluoroscopic guidance and deployed just below the renal arteries. The opening in the bifurcated module for the contralateral limb is cannulated by way of the other femoral artery and the contralateral limb is deployed to create a bifurcated stent graft that excludes the aneurysm from the circulation.

Choice of Standard or Endoluminal repair

Because the long-term outcome of endovascular repair is not yet known, young and good-risk patients with expected long-term survival are probably better served with open surgical repair. Patients requiring additional abdominal or pelvic revascularization procedures, patients with narrow femoral and external iliac access vessels, patients with a short or tortuous neck and common iliac aneurysms, and patients at risk for colon ischemia are not candidates for endovascular repair and should undergo open surgical repair (55). Endoluminal repair of AAA was first described by Parodi in 1991 (18), and has now become well established, as a favorable alternative to open surgical repair in patients with high risk for peri-operative morbidity and mortality (1,2,3). Candidates for this procedure also include patients with a proximal infrarenal neck at least 1 to 2 cm in length and common iliac arteries for proximal and distal fixation of an endograft, without excessive tortuousity and with appropriate iliofemoral access (55). The advantages of this less invasive technique which include fewer or no blood transfusion, reduced length of hospitalization, and being more appealing to the patients are offset by the uncertainty of the aneurysm sac evolution and the possibility of early or delayed complications such as graft failure, migration, kinking, thrombosis, and the development of endoleak (EL) which is considered the "Achilles heal" of this procedure, is defined as "persistent blood flow into the aneurysmal sac from within or around the graft (graft related) and from patent collateral arteries (nongraft related)" (17). This can lead to increase pressure within the native aneurysm sac leading to its expansion and eventual rupture (19,20,21). The incidence of EL reported in the literature varies widely (4-49%) and is dependent on factors related to patient selection, technical factors and duration of graft placement (10, 17, 22-28). Schurink et al. (50) performed a metaanalysis of 23 publications of endovascular aneurysm repairs encompassing 1,189 patients and reported an EL rate of 24%, with the most common site being the distal attachment. Both the significance and the natural history of ELs remain unresolved. Furthermore, it appears that the type of EL and the time course (early versus late) are of clinical significance. In the report by Matsumura and More (22) of the early experience with the Endovascular Technologies device, 47% of the 59 patients had initial ELs but 50% sealed spontaneously. The long-term integrity of the seal between the endograft and the aorta remains concerning in light of reports of continued growth and remodeling of the infrarenal cuff. Lipski and Ernst (51) analyzed 272 patients who underwent standard, open aneurysm repair and reported that the infrarenal cuff both expanded and lengthened over time. Therefore, endovascular repair may not be optimal for patients with long life expectancy or proximal aortic cuff diameter larger than 27 mm(52). The ideal outcome of endovascular repair is for the aneurysm shell to shrink or regress with time. Aneurysms that continue to enlarge after endovascular repair represent an increased risk for rupture and mandates further intervention. Similarly, aneurysms that stay at the same size is worrisome and may reflect an occult EL. Additionally, conversion from an endoluminal repair to an open repair presents several technical challenges and is associated with an increased mortality rate. Thus, unlike conventional open aortic aneurysm repair, postoperative follow-up is imperative, and likely needed for the remainder of the life of the patient after endovascular aneurysm repair. The initial clinical experience with endovascular repair has emphasized that long term follow-up with serial imaging is mandatory. Indeed, it has been reported that approximately 25% of patients will have to undergo some type of remedial procedure (54). This requirement should be factored into the decision between endovascular and standard repair. Patients undergoing endovascular repair should be sufficiently reliable to comply with the postoperative imaging protocols, which add significantly to the expense of the endovascular approach. Initially, patients with moderate renal insufficiency were discouraged from undergoing endovascular repair because of the obligatory contrast load associated with various imaging studies. However, newer imaging algorithms have been developed to minimize or eliminate the contrast exposure. The optimal algorithm for postoperative imaging in terms of both type of study and time frame remains to be determined. The imaging objectives include determining the aneurysm size, screening for ELs, and assessing changes in the configuration of the endograft. Contrast enhanced computed tomography (CECT) scan has emerged as the postoperative follow-up study of choice (gold standard) after endovascular aneurysm repair. It is believed to be highly sensitive in detecting EL and provide more accurate and reproducible aneurysm diameter measurements than duplex ultrasound (DUS) (4,5,6). However, regular, frequent, and life long follow-up. CECT scan has the following limitations:

(1) Relatively invasive.

(2) costly procedure.

(3) repeated exposure to radiation.

(4) entails the injection of contrast material that can precipitate renal failure in an already vulnerable population. This is in addition to a well-known contrast related hypersensitivity.

Duplex ultrasound (DUS) on the other hand, is a simple procedure that avoids all the above mentioned problems. It is well established as dependable tool for screening the population at risk for abdominal aortic aneurysm development and for surveillance of aneurysm diameters (29-32). Therefore, DUS is more appealing than CECT scan in the follow-up of this population of patients. However, whether it is adequate and safe will depend on how accurate it correlates with CECT scan for postoperative aneurysm sac diameter measurements and graft related complications, mainly EL detection.

Levovist:

Is an ultrasound contrast material consisting of granules that are composed of 99.9% galactose and 0.1% palmitic acid. Prior to use, Levovist must be reconstituted with sterilized water for injections and shaken vigorously for 5-10 seconds. After injection of the suspension into a peripheral vein, Levovist leads to temporary enhanced ultrasound echoes from the heart chambers and blood vessels. The distinct amplification of the ultrasound echo is caused primarily by micron-sized air bubbles, which are formed after suspension of the granules in water. Mediated by the palmitic acid additive, they remain stable for several minutes while in transit through the lungs and heart, and subsequent vascular bed before dissolving in the blood stream. General indications for Levovist use include one or two-dimensional Doppler sonographic blood flow imaging in patient with insufficient Doppler signal intensity. The drug should not be administered to patients with galactosemia. Precautions should be taken when administering the drug in children and in pregnancy because its safety has not yet been established in such patient population. No serious adverse effects were reported from clinical trials. Most were transient, and include: vasodilatation [sensation of warmth] (6.2%), injection site pain (3.9%), paresthesia (3.0%), and pain (1.4%).

Contrast –enhanced ultrasound using (Levovist) was claimed to be Comparable (16) or even superior (7) to CECT scan and routine DUS for EL detection.

Current imaging options for post-operative endoluminal abdominal aortic aneurysm (6):

Abdominal radiographs

Simple radiographs of the abdomen and pelvis are surprisingly useful studies after endovascular repair of abdominal aortic aneurysm. They are easy to obtain and are inexpensive, and they can reveal 2 of the most feared complications of endovascular surgery-endograft migration and stent deformation. Evidence of such complications must be taken seriously because they can lead to graft thrombosis, secondary EL, and even rupture. Graft migration is relatively difficult to measure precisely on abdominal films, however, and suspicion of migration is more accurately determined by abdominal CT scan. Conversely, stent-graft deformation is easier to determine from serial abdominal radiographs than from conventional CT.

The keys for appropriate abdominal radiographs are: use standardized views (eg, anteroposterior, lateral, and oblique with a reproducible, defined angle); use internal landmarks such as vertebral bodies or artificial external landmarks; have films reviewed by an experienced reviewer; and use relatively frequent intervals until more is known about the natural history of the endograft in question. The intervals may be adjusted depending on the rate of aneurysm shrinkage, the amount of change seen on prior studies, and the available data on the endograft in question. Abnormalities such as graft migration and deformation are likely to prompt further investigation, depending on the severity and the clinical setting. Regular radiographs of the abdomen should continue for the life of the patient, probably at yearly intervals even if there are no problems within the first 2 years.

Duplex scanning

At most centers duplex scanning is an adjunctive study for postoperative follow-up after endovascular AAA repair. Duplex scanning have the advantage of being relatively inexpensive and noninvasive, and it delivers no ionizing radiation or ionized contrast. Duplex scanning can detect ELs, limb stenosis, occlusion, and significant pathological conditions in the native aorta, visceral vessels, and iliac arteries. Duplex scanning also can be used to follow maximum AAA diameter. The problem with duplex scanning is that many patients have large abdominal girth, and imaging of the key areas may be quite limited. Duplex scanning is also highly dependent on the experienced of the technologist. Current reports indicate that the accuracy of duplex scanning for detection of EL is on the order of 80% to 85%, and there is much higher incidence of indeterminate studies for duplex scanning than for CT scan (12). Some investigators believe that duplex scanning using an intravenous contrast (levovist) is comparable to CT for detection of EL (16), but most think that CT is superior. Even with intravenous contrast, some ELs can be missed on duplex scanning and detected on CT. CT is also known to have greater accuracy and less inter-observer variability for the crucial measurement of aneurysm diameter (4, 5). Duplex scanning is still useful as an adjunctive study, however. The primary role of duplex scanning is to investigate suspected abnormalities in the pelvic or visceral vessels, to evaluate patients with renal insufficiency, and possibly, to reduce the frequency of CT in selected patients.

Computed Tomography (CT)

The CT scan is the standard postoperative study after endovascular aneurysm repair. It is believed by most to be more sensitive in detecting ELs than Duplex scanning (DUS) (4, 5). Spiral CT is much preferred over conventional CT, for a number of reasons.

Because spiral CT is capable of fine collimation (thin "cuts", or narrow width of the of the x-ray beam), reconstruction interval in the order of 2 mm, multiplaner reconstructions (coronal, sagital, curvilinear), and three dimensional (3D) reconstructions. Using a CT workstation with specialized computer software, highly magnified views of axial reconstructions or multiplanar reconstructions can be viewed in rapid sequence, allowing one to "track" a suspected EL to potential inflow and outflow sources. The latter technique is far superior to simple review of selected hard-copy images, where subtle ELs are easy to miss. All these features are also critical for the evaluation of visceral, iliac, and renal occlusive disease. The combination of spiral CT and multiplanar reformatting is often referred to as CT angiography (CTA) or contrast enhanced CT, and this technique can be quite accurate in evaluating the extent of aortic aneurysms, the presence of visceral aneurysms, and the presence of occlusive disease in the aorta and its branches.

CT is less technology dependent than DUS, but nevertheless requires training, experience, and case-specific planning to obtain quality studies. Any new EL, or expansion of the aneurysm should be taken very seriously because of the risk for rupture. CT scan surveillance should continue for the life of the patient, probably on a yearly basis, if there are no apparent problems.

Magnetic resonance angiography

MRA is gaining increasing acceptance for cerebrovascular and infrainguinal peripheral vascular occlusive disease. It is not commonly used for the evaluation of patients after endovascular AAA repair, however. Disadvantages include increased cost, a proportion of patients are claustrophobic, and metal used in endografts can cause significant artifacts on MRA studies. More importantly, MRA provides relatively poor display of intraluminal thrombus and calcified plaque. Therefore, the role of MRA in this area is likely to be limited.

Arteriography

In general, arteriography is only used postoperatively when known endoleak is evaluated for endovascular treatment or when endoleak is suspected because of aneurysm expansion without demonstration by other studies.

Intravascular ultrasound

Intravascular ultrasound (IVUS) is invasive, so its role is usually limited to cases of known or suspected endoleak.

<u>The purpose of this study</u> is to examine:

(1) the accuracy of DUS as compared to CECT scan with regards to aneurysm sac diameter measurements and endoleak (EL) detection in the follow-up of patients with endoluminal repair of abdominal aortic aneurysm.

(2) The value of contrast enhanced ultrasound (levovist) as compared to routine DUS for EL detection.

MATERIALS and METHODS

This is a prospective non-randomized blinded study. Between February 1998 and December 2000, all patients who underwent successful endoluminal repair of AAA at the McGill University Health Center were prospectively evaluated by contrast enhanced computed tomography (CECT) scan and a duplex ultrasound (DUS)examinations in their post-operative follow-up. Importantly, CECT scan is considered nowadays the "gold standard" in the fo llow-up of endoluminally repaired AAAs. DUS, on the other hand, is used in cases where the CT scan finding(s) are unclear or doubtful so that to rule out or confirm a suspicious finding. Hence DUS use is not a routine one in patients' follow-up. The addition of DUS to the follow-up protocol did not expose the patients to any risk (such as radiation, or renal toxicity), therefore additional consent was not obtained. At one hospital, patients also underwent contrast-enhanced ultrasound using levovist injected intravenously. Both DUS and CECT were looking at the maximum antero-posterior (AP) and transverse (T) diameters of the aneurysm sac, and the presence or absence of EL. While levovist DUS and routine DUS compared EL detection only. At the end of each u/s examination, information relative to the study were recorded on a special data collection sheet by the radiologist performing the exam. DUS exams were rated as good, limited, or poor. Data on DUS examination findings were gathered from a special data sheet after discussion with the radiologist who performed the exam, and data on CECT scan findings were obtained from the final scan reports and discussion with an experienced radiologists.

The radiologist performing the CECT was unaware of the ultrasound result and vice versa.

At one hospital, all CECT scans were read by and discussed with a single experienced radiologist. In a similar manner, all DUS exams were performed and reported by a single radiologist familiar with the endovascular technology. At the other hospital, all CECT scans were read by and discussed with an experienced radiologists. Most (85%) exams were performed and read by a single radiologists, for the remainder, however, two other radiologists were involved.

Demographic data were obtained by the primary investigator (myself) from patients' hospital charts during the period of the study.

Exclusion criteria :

1- Patients who were followed-up elsewhere.

2- Patients who were followed-up by CECT scan only (no DUS performed).

3- If the concurrent (paired) study was done more than one month apart.

4- Studies where CT scan was done without contrast were excluded from endoleak detection comparison.

. <u>Imaging Protocols:</u>

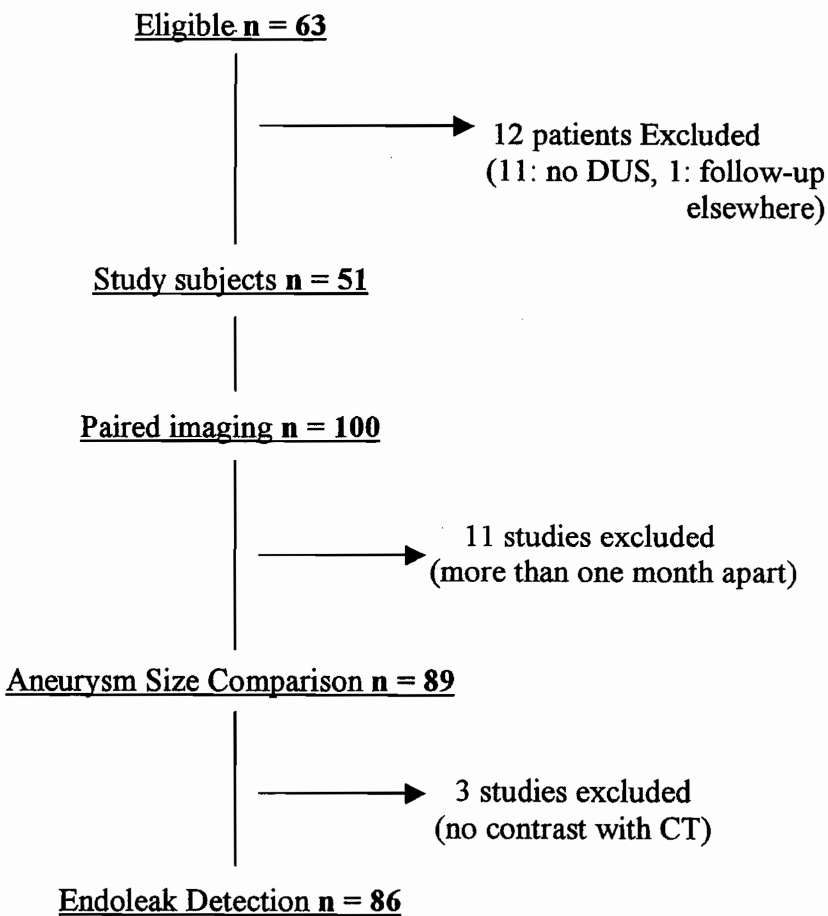
CT: There was a slight difference in the CT scan and ultrasound protocols in the two hospitals. At one hospital, the contrast enhanced ct scan was performed using a Picker CT Twin Flash Spiral Helical Unit, a pitch of two, slice thickness of 3.2 mm, with an increment of 1.6 mm. a total intravenous contrast of 150 cc were injected at a rate of 4 cc/second. Image acquisition was started 15-25 seconds after contrast injection. Aortic aneurysm sac was measured in both the axial and the aortic plane. At the other hospital, the CT scan was performed using a Seimens Plus 4 machine, a pitch of one 10 x 10 mm, or a pitch of one and a half 0.8 x 1.2 mm, reconstruction every 0.7 mm. A total of 100-150 cc of intravenous contrast was injected with a power injector at a rate of 1.5 cc/second. Image acquisition started 60-70 seconds after contrast injection. Aortic aneurysm sac was measured in both the axial and the aortic plane. In both hospitals CT scans were reviewed and reported by an experienced radiologist. An EL was defined as persistent blood flow between the stent graft and the walls of the aneurysm. This was further divided into type one endoleak when it resulted from leakage around the proximal or distal ends of the graft or at the junctions between modular stents, and type two EL when the blood flow in the native aneurysmal sac is caused by collateral vessels from lumbar arteries and/ or inferior mesenteric artery (17). On CECT an endoleak was characterized by extravasation of contrast dye between the prosthesis and the aneurysmal wall.

DUS: In both hospitals, there were no special dietary instructions to the patients to follow for the day before the examination. "ATL 5000", and occasionally "Toshiba 6000" machines were used. Ultrasounds were done with a 3 MHz curved probe or a 10 MHz linear probe depending on the body habitus of the patient. Gray scale was used for aneurysm diameter measurements (in the plane of the aorta). A color doppler (duplex) was used for detection of endoleaks which were characterized by detection of a colour and spectral signal outside the limits of the prosthesis. In one hospital, Levovist (galactose-palmitic acid) was injected after the completion of the ultrasound exam and the above steps were repeated except for aneurysm diameter measurements.

Statistical methods

The sample size was estimated using Pearson's correlation. A sample size of n = 75 (number of concurrent studies) was estimated for the study to have a power of 0.8 at 0.05 level of significance. Based on our sample size of n=86, and specifying a clinically relevant difference of 15% between the two endoleak detection imaging modalities with 5% false negatives, at a 95% level of significance, this study achieved a power of 92% (8). The Paired Student T-test (56) was used to compare differences in aneurysm diameter measurements, and Kappa statistics (57) was utilized to compare the level of agreement between imaging modalities in the study.

RESULTS



As shown in the above figure, a total of 63 patients were eligible for the study, 12 patients were excluded; one for elsewhere follow up, and 11 patient who simply did not have DUS in their follow up. The remaining 51 patients had a total of 100 paired studies, 11 of which were excluded from analysis because more than one month had elapsed between the concurrent exams. Of the 89 paired studies that were analyzed, 3 were excluded from EL detection comparison because no contrast was used in CECT scan (clinically contra-indicated).

Fifty one patients made the study sample, 28 were operated on and followed at the Royal Victoria Hospital and 23 were operated on and followed at the Jewish General Hospital. Fourty five were males and 6 were females, with a mean age of 76.6 years and an age range of 59 to 92 years. Close to 18% were obese and about two third had coronary artery disease and one third smoked cigarette. A bifurcated graft was used in just over 90% of patients. Table (1) describes the characteristics of the study sample (next page).

Table (1)

Demographic data

Variable	N	%
Hospital:		
Royal Victoria	28	54.9
Jewish General	23	45.1
Gender:		
Male	45	88.2
Female	06	11.8
Age (year):		
Mean +/- SD	51	76.6+/- 7.6
Range		59-92
Obesity	09	17.6
Coronary Artery Disease	33	64.7
Congestive heart failure	04	07.8
Hypertension	30	58.8
Diabetes Mellitus	04	07.8
Chronic Obstructive Pulmonary Disease	14	27.5

Dyslipidemia	13	25.5
Cerebro-vascular Accident	08	15.7
Cigarette smoking	17	33.3
Chronic Renal Failure	4	07.8
Graft Name:		
Vangard	19	37.3
Talent	31	60.8
Zenith	01	02.0
Graft Type:		
Bifurcated	46	90.2
Uni-Iliac	05	09.8

When comparing **aneurysm diameters measurement**, we found that on average aneurysm size measured by CECT scan is greater than those measured by DUS by about 2.5 mm or less. This difference was consistent, and therefore, although statistically significant, it was clinically acceptable as the change in aneurysm diameter over time is clinically relevant (table-2a). Stratification by obesity, hospital, and quality of ultrasound did not significantly change our results. In addition, there was a high correlation between the two modalities when we compared the change in aneurysm diameters measurement between the first and second (r for AP = 0.7, r for T = 0.3), and the second and third follow-up exams (r for AP = 0.9, r for T = 0.8) (table-2b). It is worth mentioning that although the maximum AP and T diameters of AAA are routinely measured, it is the AP diameter that is more accurate and therefore more reliable and clinically relevant. This is simply due to the fact that aneurysm tortuosity makes it difficult to rely on the T diameter.

Table (2a)

CT VS U/S: Aneurysm Diameters Measurements:

Diameter measured		Difference (CT-US) in Aneurysm diameter size (cm)	
	N	Mean (SD)	p-value(*)
AP	89	0.25 (0.34)	0.001
T	89	0.23 (0.44)	0.001

(*) Results of paired Student t-test.

Table (2b)

.CT VS U/S: Comparing Aneurysm Diameter <u>Changes:</u>

		CT measurements			
		FU2-FU1 (n=25)		FU3-FU2 (n=12)	
US measurements		AP	T	AP	T
FU2-FU1	AP	0.7			
	T		0.3		
FU3-FU2	AP			0.9	
	T				0.8

NOTE: Content of this table represents Pearson product-moment correlation coefficients.

When comparing CECT scan to DUS for **endoleak detection** (table-3) in 89 concurrent studies, 3 were excluded from the analysis because no contrast was used in CT scan which left us with a total of 86 concurrent studies available for analysis. DUS had a sensitivity, specificity, positive and negative predictive values of 50%, 86.7%, 61.9%, and 80% respectively. Based on kappa statistics (simple kappa coefficient and confidence interval), the agreement between the two modalities was 0.4 (0.2-0.6). This agreement is considered moderate and was statistically significant (p-value<0.05). This agreement was not significantly affected when stratified by obesity, hospital or quality of DUS.

Table (3)

CT VS DUS: Endoleak Detection

	EL on CT		
EL on U/S	YES	NO	TOTAL
YES	13	8	21
NO	13	52	65
TOTAL	26	60	86

Sensitivity = 50%

Specificity = 86.7%

Positive predictive value = 61.9%

Negative predictive value = 80%

Kappa method of agreement (Confidence Interval) = 0.4 (0.2-0.6).

There were 21 **discrepancies** between CECT scan and DUS (table 3): 13 cases where CT scan showed endoleaks undetected by DUS, and 8 cases where DUS showed an endoleak undetected by CECT scan. When looking at discrepancies in terms of **aneurysm growth** (aneurysm growth was defined as an increase in antero-posterior (AP) diameter on CECT scan by more than 2 mm), non of the 3 occasions were detected by DUS (table-4a).

Table (4-a)

CT, U/S discrepancies in Endoleak detection in relation to <u>aneurysm growth</u>

<u>Aneurysm Growth</u>

	Yes	No	Total
EL on CT only	3	10	13
EL on U/S only	0	8	8
Total	3	18	21

Note: All three occasions were aneurysm expanded were detected on CT scan only.

When aneurysm growth was examined in relation to **type of endoleak** (table-4b) we found that 1 of 3 aneurysm with type-1 endoleak increased in size, while only 2 of 18 aneurysms with type-2 endoleak had actually expanded. In addition, each of the 3 aneurysms that increased in size belonged to a different patient.

(Table-4b)

- **Aneurysm growth and endoleak type**

	Aneurysm Growth		
	Yes	No	Total
Type-1 EL	1	2	3
Type-2 EL	2	16	18
Total	3	18	21

Note:

1- One of 3 type-1 EL increased in size.

2- Two of 16 type-2 EL increased in size.

3- Each of the 3 aneurysms that increased in size belonged to a different patient.

Table (4-c)

CT scan, U/S discrepancies in Endoleak detection compared to <u>type of Endoleak</u>

Endoleak	Type-1	Type-2	Total
On CT only	3	10	13
On U/S only	0	8	8
Total	3	18	21

Note: All three type-1 endoleaks detected on CT scan were missed on ultrasound.

Table (4-d)

CT scan, U/S discrepancies in Endoleak detection compared to <u>type of endograft</u>

Endoleak	Uni-iliac	Bifurcated	Total
On CT only	2	11	13
On U/S only	0	8	8
Total	2	19	21

<u>Note</u>:

1- The 2 occasions where U/S missed an EL in a uni-iliac graft was in the same patient (EL located posterior to graft limb).

2- 11 of 13 occasions where only U/S missed an EL were in bifurcated grafts.

When comparing routine DUS to contrast (levovist) enhanced DUS, 38 concurrent exams in 28 patients were available for analysis (table 5). Results showed kappa coefficient of 1.0 with a confidence interval of 1.0-1.0 that's to say: perfect agreement. In other words, there was no one case that levovist DUS detected an endoleak that was missed on routine DUS and therefore, levovist DUS did not improve the accuracy of routine DUS.

Table (5)

Duplex ultrasound versus Levovist Duplex ultrasound: <u>Endoleak Detection</u>

EL on ultrasound	EL on levovist ultrasound		
	PRESENT	ABSCENT	TOTAL
PRESENT	7	0	7
ABSENT	0	31	31
TOTAL	7	31	38

Note: A perfect agreement between the two methods.

DISCUSSION

This is a prospective nonrandomized blinded study comparing duplex ultrasound to contrast enhanced CT scan in the follow-up of patients after endovascular repair of abdominal aortic aneurysm. In a blinded fashion, both imaging modalities were compared with respect to aneurysm diameter measurement maximum (AP) and (T), and the rate of endoleak (EL) detection. Our study also compared the use of routine DUS to contrast enhanced (levovist) DUS in the same population of patients for EL detection rate.

Our study demonstrated several areas of ***Strength*** including:

1- Its' inherent design.

2- The fact that our radiologists performing one type of imaging modality were blinded to the results of the other modality and vice versa.

3- The number of radiologists performing one imaging modality was limited to one (sometimes two) in the overwhelming majority of exams. This resulted in a reduction in inter-observer variability leading to more reliable results. Reliability was also enhanced by the study specific and well-defined outcome variables measured on each imaging modality.

4- All radiologists performing the imaging tests are experienced, thorough, and familiar with the endovascular technology.

Findings and possible explanations:

Duplex ultrasound was accurate and reliable in measuring aneurysm diameters despite under-estimating diameters by an average of 2.5 mm because this was consistent. On the other hand, it only moderately agreed with CECT for EL detection. There were 21 discrepancies between the two imaging modalities in our study: 8 occasions where DUS showed an endoleak undetected on CECT, and 13 occasions where CECT showed ELs undetected on DUS. At the end of the study period, these discrepancies were reviewed with the radiologists in an attempt to know why they existed in the first place.

We postulated two possible explanations for ELs detected only on DUS:

1- Either too small to be detected on CT or minor calcifications in the wall of the aneurysm (five occasions)

2- Small but definite ELs simply missed on CT (three occasions).

We postulated five different explanations for ELs detected only on CT scans (for examples please see appendix) :

1- Missed on DUS because they were located directly behind the metal stent, and therefore, the wave forms did not penetrate through but reflected of the stent (five occasions). Of note, this constituted the majority of EL undetected by DUS. Interestingly, this observation was pointed out in a previous report (15).

2- What was felt to be EL on CT was thought to be small bulges on the stent graft (four occasions).

3- Short, linear ELs, peripheral in location not picked-up because the sound waves were perpendicular to the direction of the endoleak (two occasions). This can be avoided in the future by more vigilant exams, taking care to attempt scanning from all possible angles.

4- One occasion where the EL was very small possibly an artifact.

5- One occasion where DUS missed a large pelvic (distal) type one EL. The patient was taken back to the operating room and underwent a successful extension endograft insertion. This incident happened early in the study period and can be attributed to the relative unfamiliarity of the ultrasonographer with the relatively new endovascular technique at our institution.

The study, however had the following ***Limitations:*** 11 of 63 patients(17.5%) eligible for the study were excluded for they were followed-up only by CECT scan. This resulted partly from failure of personnel to comply with the study protocol in the initial period, and partly due to radiology scheduling (booking) difficulties since the system in our institution is stretched to the limits.

Results and findings of other similar studies / comparison and possible explanations for differences in results:

Earlier in the endovascular era, several reports on aortic endograft trials have only included endoleaks diagnosed with CT scans and have ignored evaluation with DUS (9, 10, 11). Several research groups had studied the role of DUS in the postoperative follow up of endoluminally repaired AAA patients, some compared it to CECT scan (CT/angio), and some did not.

In 1998, Sato et. al. compared endoleak detection rate for DUS and that of CECT scan with excellent results (sensitivity = 97%, and negative predictive value = 98%). The study had poor specificity (74%), and positive predictive value (66%), and a relatively high incidence of indeterminate DUS studies (12%). This was attributed to the suboptimal technical evaluation. With improvements in DUS imaging, some of the false positives when compared with the a CT imaging may truly represent endoleaks. This was suggested with the reexamination of the videotaped studies with DUS that showed an EL present, and CTs that showed an EL absent. Heilberger et al. (16) also discovered that DUS can identify ELs from branched vessels that were missed on CT scan. The DUS allows a real-time sampling of the AAA sac and provides a dynamic rather than static picture. These advantages could potentially make DUS scanning more reliable than CT for the evaluation of the origin and extent of the EL. The author concluded that duplex ultrasound could potentially be equal or superior to CT scan as an accurate diagnostic tool for detecting ELs (12).

A similar results were obtained by Wolf et al in 2000 who also included a comparison of aneurysm diameter in their study and had all concurrent exams (DUS/CECT) separately reviewed by a panel of both radiologists and vascular surgeons (13). The author pointed out that the problem with this type of study is the lack of an ultimate gold standard. They also found that the number of ELs identified on CT and missed on DUS scans exceeded the number of those identified on DUS scans and missed on CT. However, none of the ELs for which the discrepancy in the diagnosis existed was judged severe enough to warrant arteriography and intervention. Although the eventual outcome of various types of ELs has not been conclusively defined, their policy has evolved to investigate and treat those that originate at the attachment sites or in the graft and those that are associated with increase in size of the aneurysm sac. Patients with ELs that appear to be related to a branch vessels without aneurysm expansion are observed. The desirable sensitivity of a useful follow-up study for identifying ELs is ultimately related to their natural history. If a branch vessel related ELs are inconsequential unless associated with aneurysm sac expansion, missing these ELs is irrelevant, and a test that visualizes EL every minute is unnecessary. In their study (13), in all patients with ELs that were thought to involve the attachment sites and to warrant arteriography and reintervention, DUS demonstrated the EL whenever it was performed. Thus reliance on duplex scan alone would not have resulted in different clinical management. Hence, on the basis of their findings, Wolf et al concludes that a well performed duplex scan delivers results very similar to high quality CT angiography. D'Audiffret et al in their report in 2001 found DUS to be 96% sensitive, 94% specific, with 98% negative predictive value when compared to CECT scan for postoperative EL detection, and less accurate for aneurysm diameter measurement in spite of fairly good correlation (73% of exams) for evolution of native aneurysmal sac. In this study, however, radiologists interpreting one imaging modality may have been aware of the result of the other concurrent exam, i.e. blinding was absent. In addition, the presence and origin of EL was agreed upon by the entire radiosurgical team. They emphasize that the examinations were performed by highly trained physicians accustomed to patients with endoprothsesis. In spite of that, in 4.5% of cases, there was a lack of agreement between the two imaging modalities which may have had a potentially serious consequences. The reasons for such discrepancy are speculative. Inter-observer variability, poor patient preparation, overweight patients, and lack of aneurismal wall echogenicity may lead to duplex ultrasound inaccuracy in some cases. In addition, postoperatively, the absence of wall motion after successful aneurismal exclusion may increase the difficulties of the measurement. On the other hand, measurement based on CT scan are not currently corrected for the axis of the aorta, which may overestimate the true aortic diameter. The use of an electronic caliper directly on the CT workstation may increase the accuracy of the aortic diameter measurements and possibly result in better correlation with duplex ultrasound (14).

Another report in 2001 by Pages et al obtained similar results to our study; for EL detection the sensitivity, specificity, positive and negative predictive values were 48%, 94%, 74%, and 81%, respectively. Aneurysm diameter measurements and evolution of aneurysmal sac correlated well between duplex ultrasound and contrast CT scan. In their series, DUS detected 5 ELs that were not observed on CT scan. One explanation they site for these false positives is that all of their contrast enhanced CT scans were performed immediately after injection without delayed sequences. Nonetheless, the finding that duplex scan can detect ELs missed by a CT scan suggests that combined use of these two modalities could improve the quality of surveillance after aortic endografting. Conversely, in > 50% of cases in their series, DUS failed to detect ELs detected by CT scan. The explanation for this high false negative rate is unclear. This findings raises questions not only about the value of DUS scanning for endostent surveillance but also about the conditions under which the procedure was performed. In this regard, they were surprised to observe that most undetected ELs were located near the aortic bifurcation, which is usually readily visualized using DUS. The authors concluded that duplex ultrasound is less reliable than contrast CT scan for surveillance of abdominal aortic aneurysm after endografting for its insufficient ability to detect ELs (15).

One technique was suggested to improve EL detection by DUS is the use of an intravenous substance that can enhance echogenicity. This had been advocated by several authors (7, 6). In the report by Mc Williams et al, one of three cases of EL was detected by DUS. When the examination was performed using Levovist contrast material, all three ELs were detected. Moreover, contrast ultrasound detected six ELs not revealed on CT scan. The authors concluded that the use of contrast enhanced (Levovist) ultrasound could become the gold standard modality for detection of EL. In our study, routine duplex ultrasound was followed by Levovist duplex ultrasound on 38 occasions and read by the same radiologist. Levovist ultrasound did not reveal any new EL undetected by routine duplex ultrasound. In other words, it did not add to its accuracy. Considering the cost and time, we believe that there is no benefit obtained from adding Levovist to routine DUS scanning.

CONCLUSION and RECOMMENDATIONS

Duplex ultrasonography had **comparable accuracy** with contrast enhanced computed tomography for evaluation of aneurysm **diameter measurement** following endoluminal repair of abdominal aortic aneurysm. There was **only moderate agreement** between DUS and CECT for **detection of endoleaks**. CECT was more reliable for detecting ELs associated with aneurysm growth. Contrast enhanced (Levovist) duplex scanning **did not change the accuracy** of DUS for detection of ELs.

Therefore, based on the results of our study, we recommend to continue using duplex ultrasound as an adjunct only and not an alternative to contrast enhanced computerized tomography scan in the follow up of endoluminally repaired AAA. We do not believe, however, based on our results, that contrast enhanced duplex ultrasound can improve the accuracy of routine duplex ultrasound for endoleak detection.

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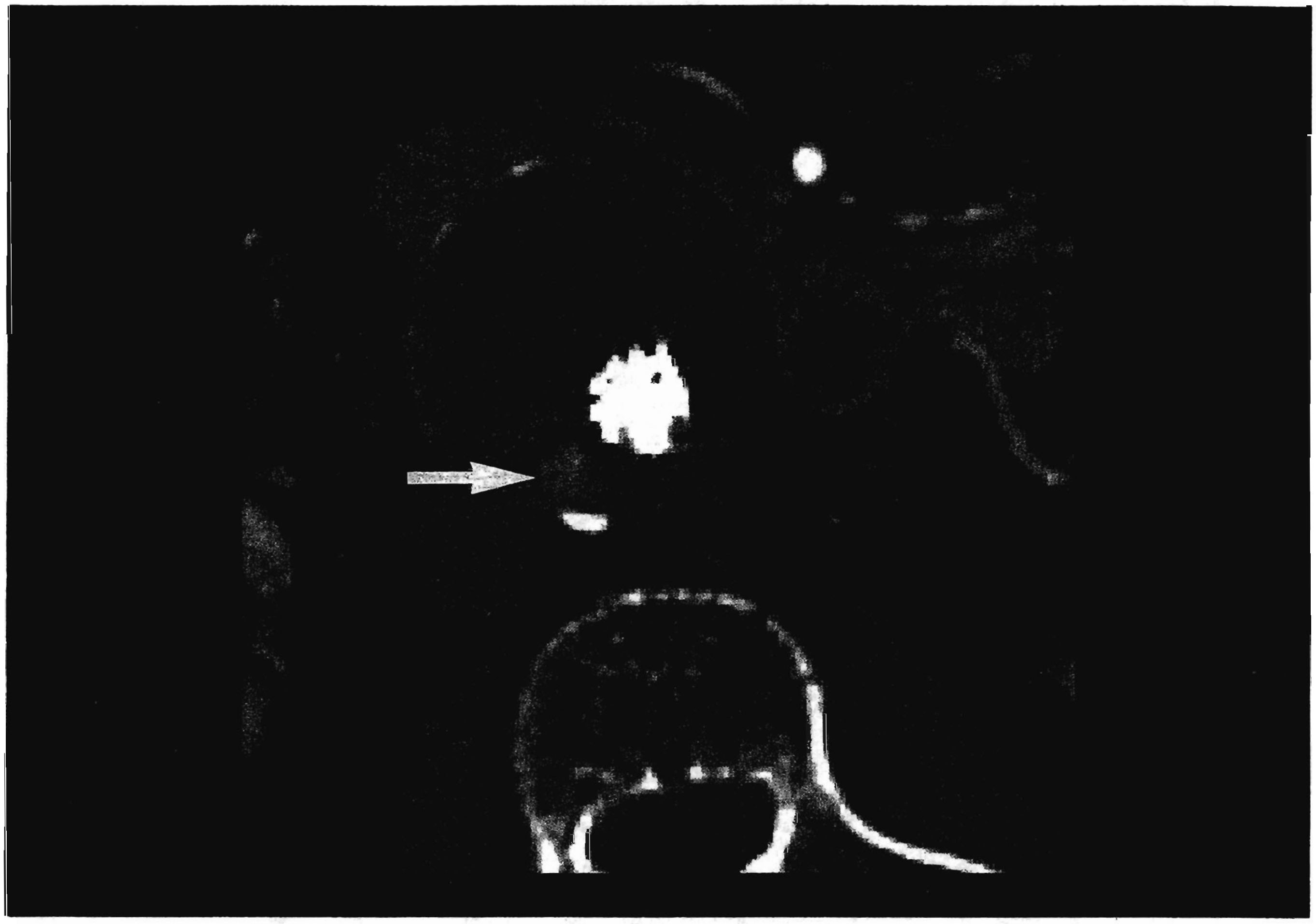
Appendix

Examples of endoleaks detect on contrast enhanced CT scan and missed by duplex ultrasound

Figure (1) Mr. S.J.

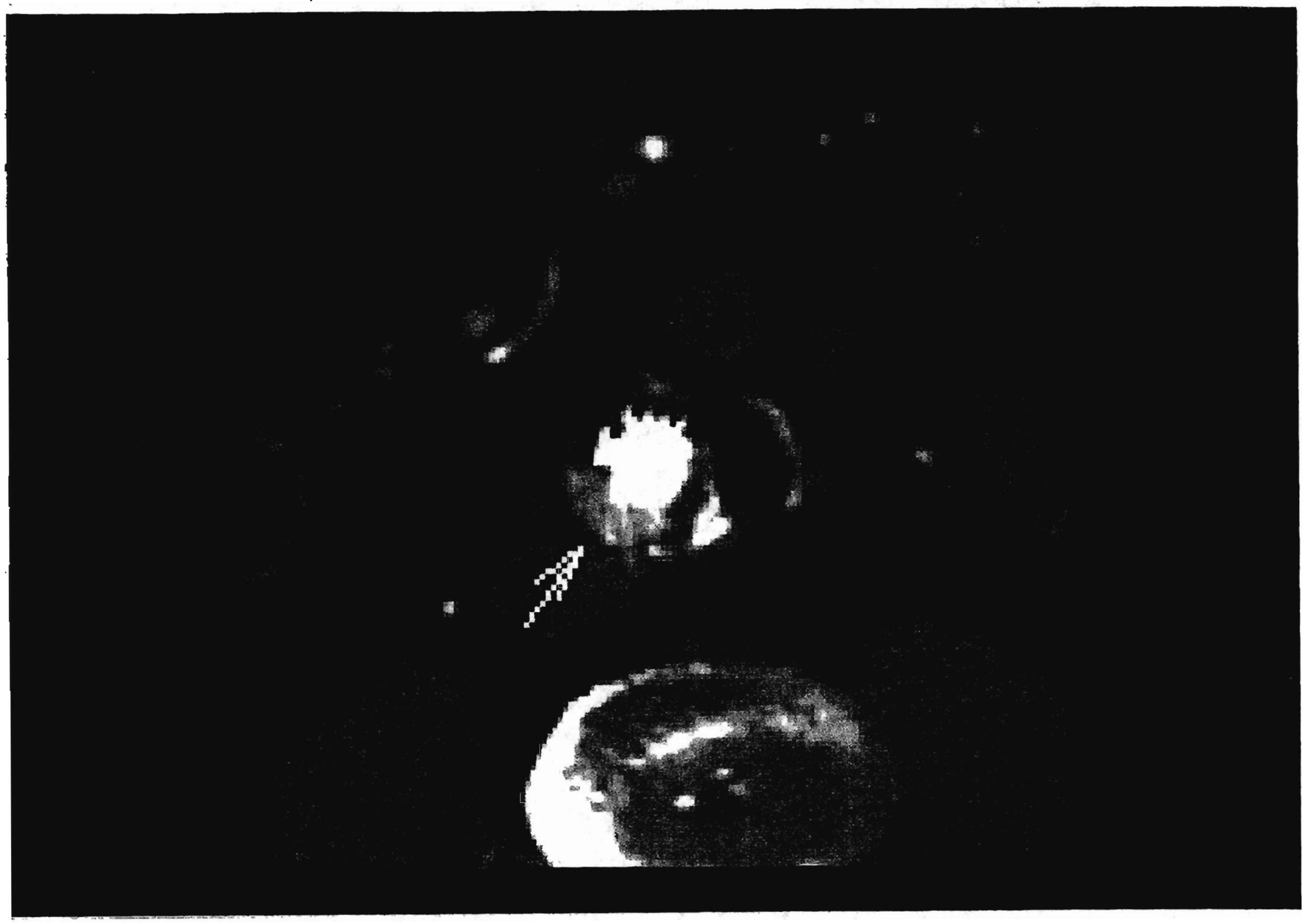
CT scan 6 months postoperatively:



There is a perigraft leak (type-2) demonstrated in the right posterolateral aspect of the aneurysmal sac adjacent to the graft. No expansion noted in aneurysm size.

Figure (2) Mr. S.J. (the same patient in figure one)

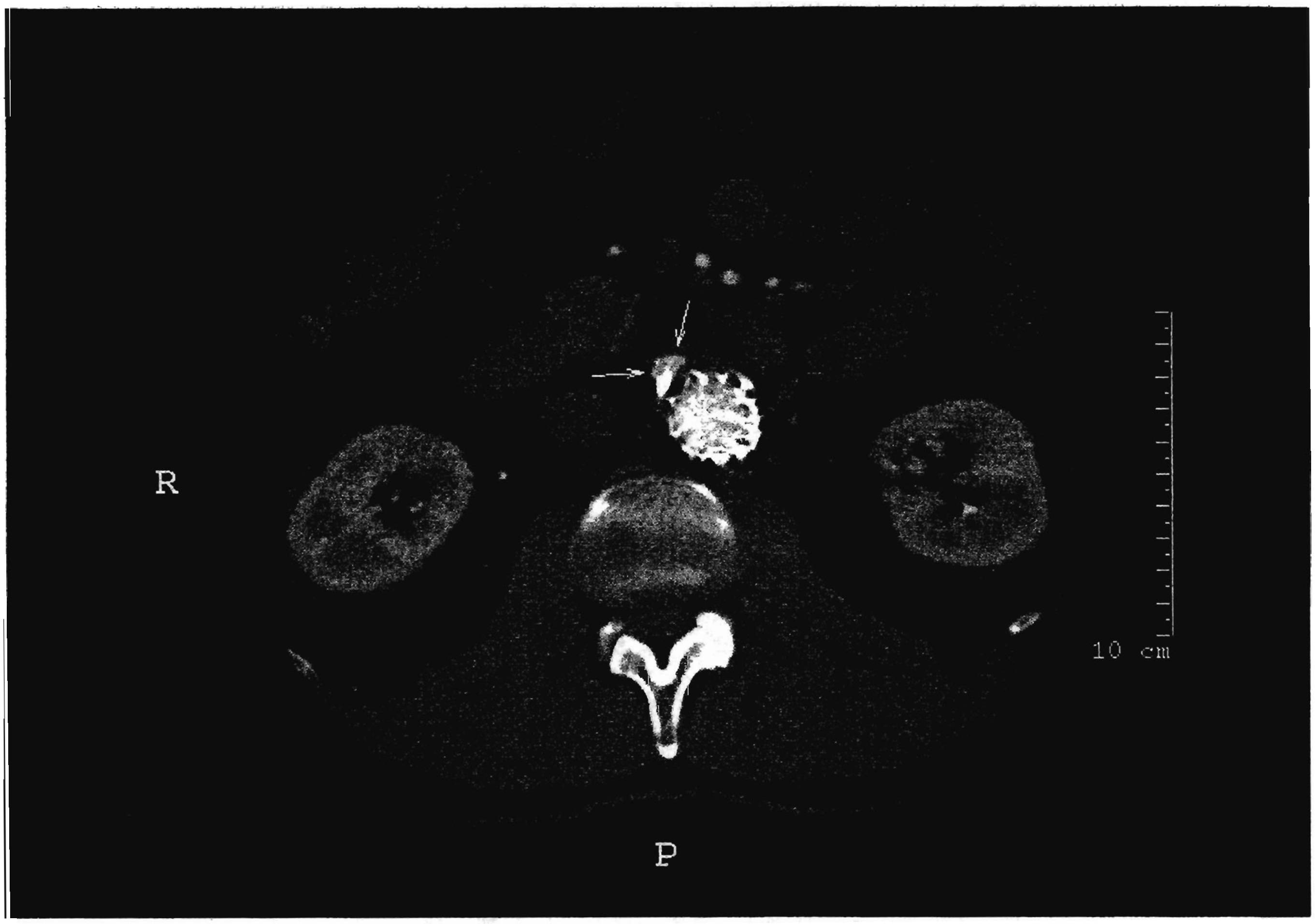
CT scan 18 months postoperatively:



Once again, there is a small type-2 endoleak in the right posterior aspect of the caudal portion of the aneurysm sac. Similar to previous. At this point there is minimal increase in aneurysm size.

Figure (3) Mr.J.B.

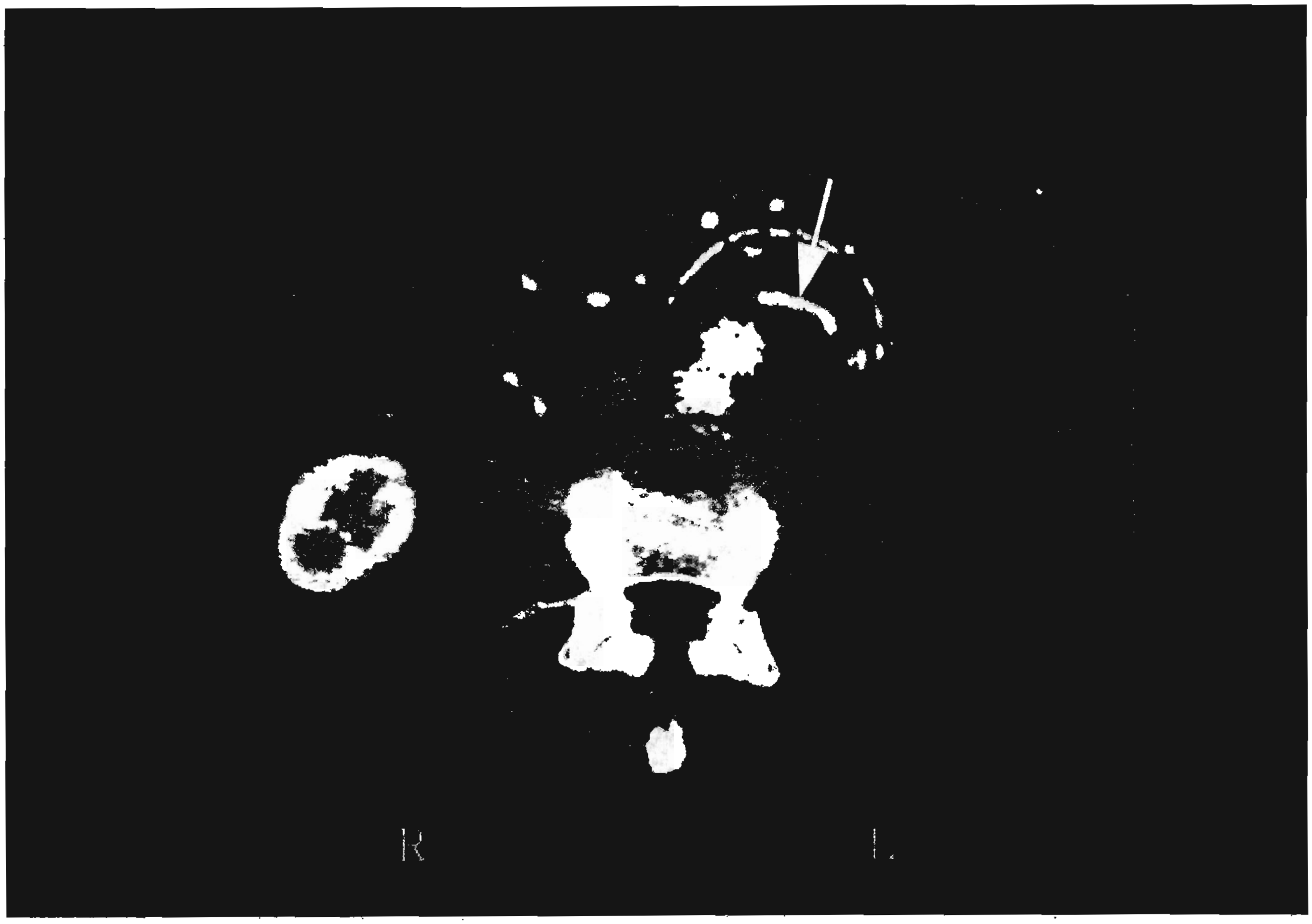
CT scan 29 months postoperatively



Anteriorly and to the right of the aortic graft there is a small contrast collection. At this point in time there is no increase in aneurysm size.

Figure (4) Mr. G.S.

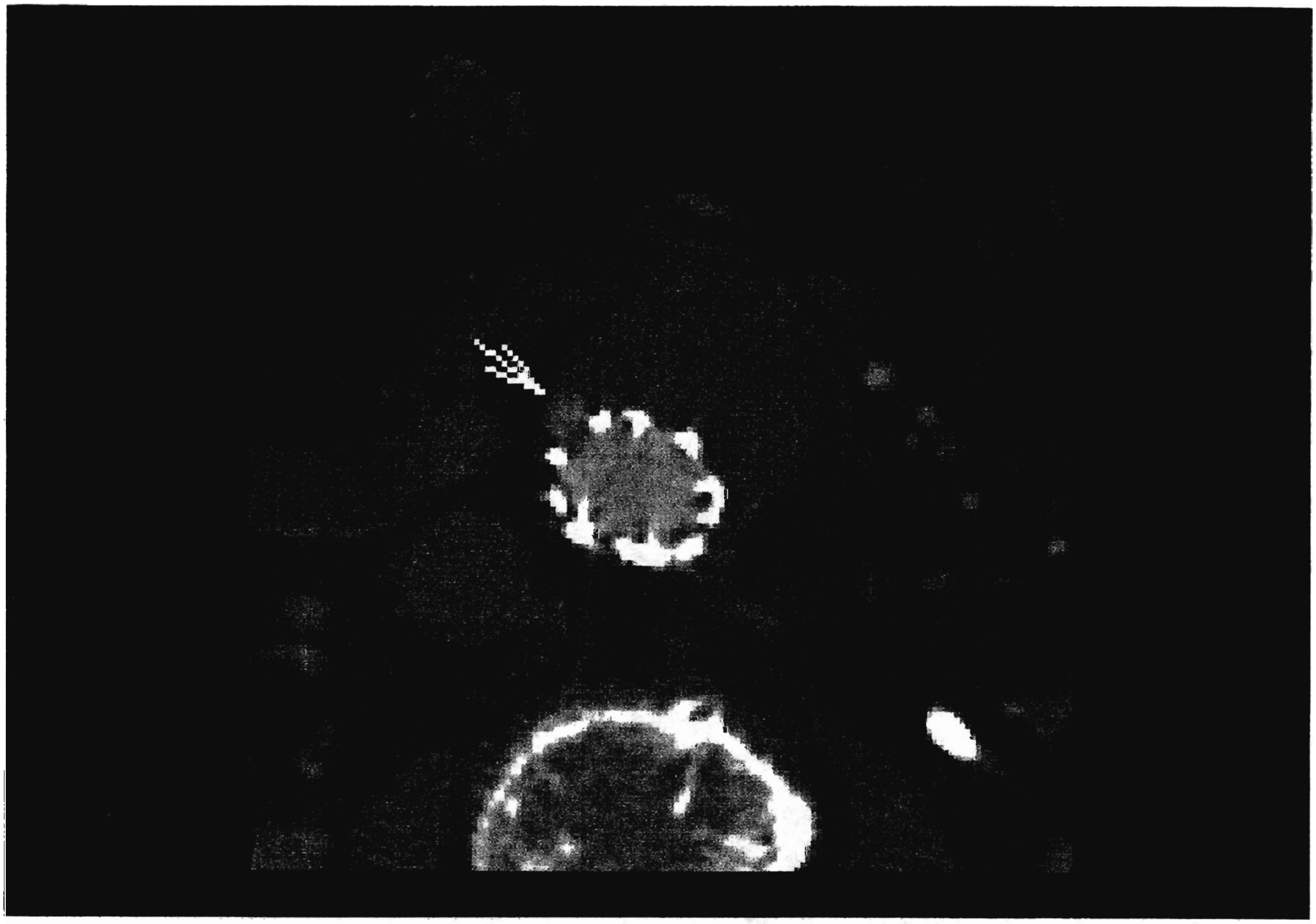
CT scan 6 months postoperatively:



There is an extravasation of contrast demonstrated within the abdominal aortic aneurysmal sac type-2 endoleak. Serpiginous contrast column. No growth of aneurysm sac.

Figure (5) Mr. J.U.

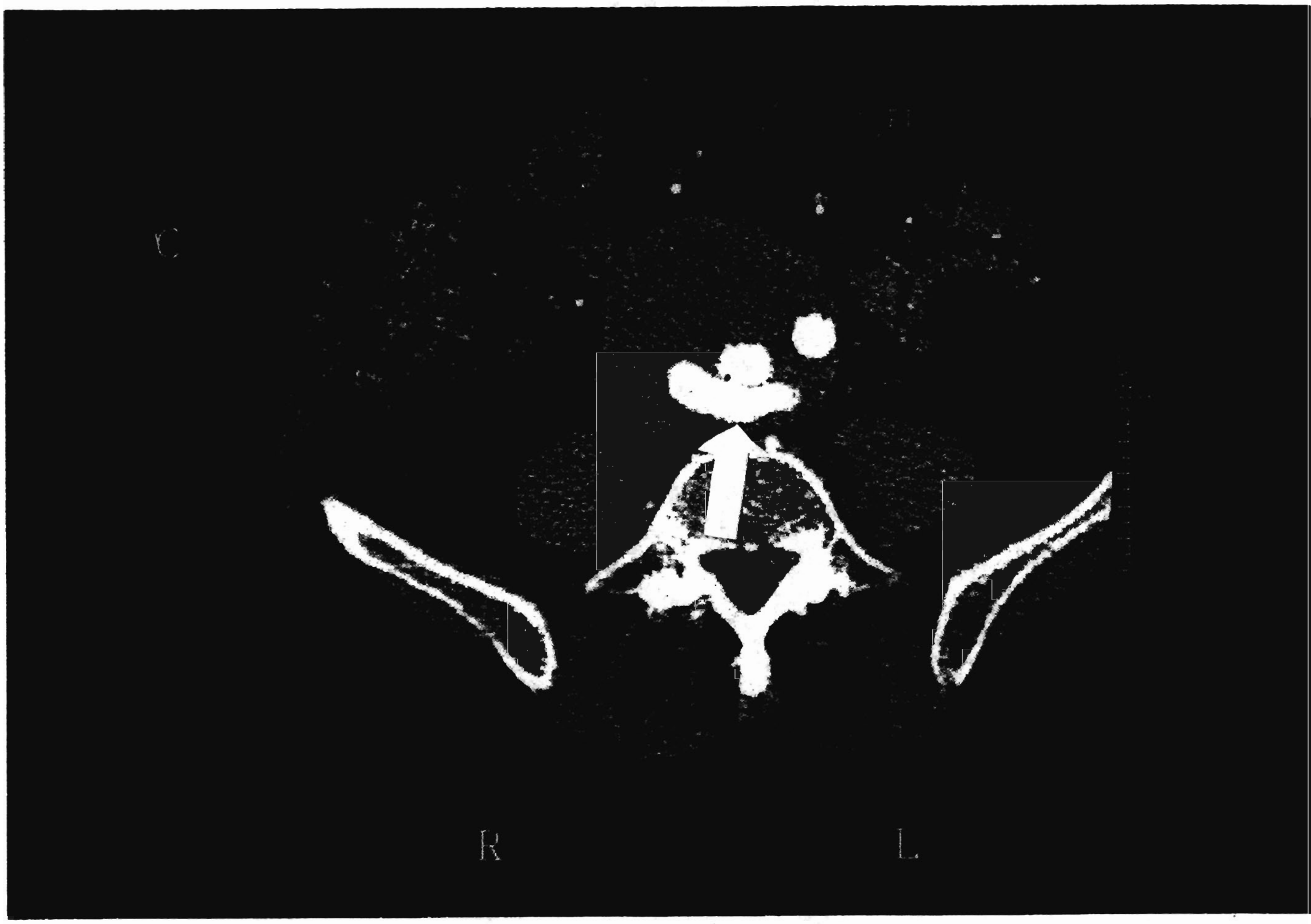
CT scan 7 days postoperatively:



There is a tiny focal region of high density, representing contrast adjacent to the proximal graft situated anteriorly and to the right. (type-1 endoleak).

Figure (6) Mr. I.C.

CT scan 24 months postoperatively:

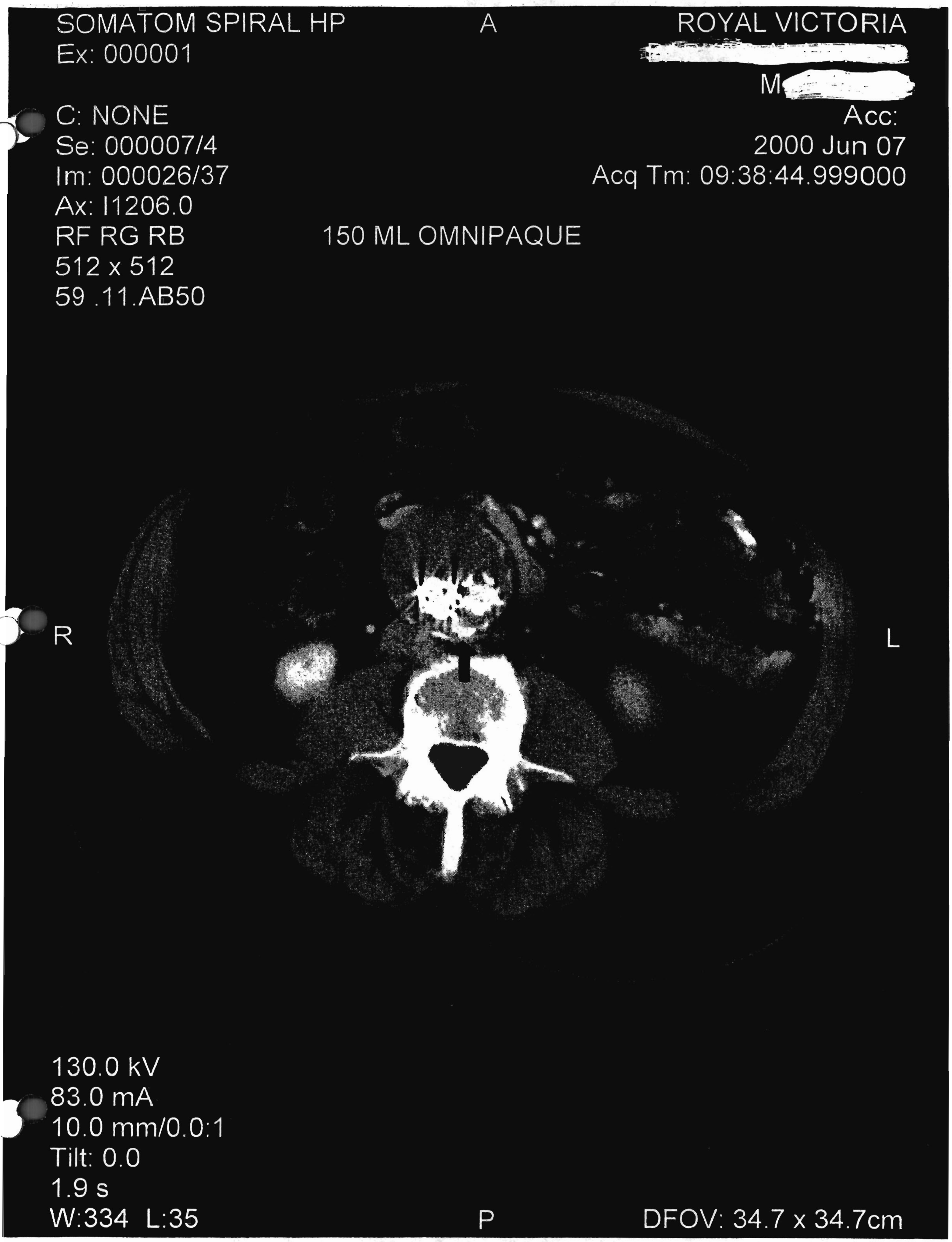


There is a large leak (type-1) in the distal aneurysm sac extending to the region of the iliac bifurcation. The limbs of the graft do not have very deep purchase into the iliac artewries, especially on the left and this is suspected to be the source of the large endoleak. Expansion of the native aneurysm sac noted.

Figure (7) and figure (8) Mr A.B.

CT scan 7 and 13 months postoperatively, respectively (next two pages):

Demonstrating contrast extravasation posterior to the endograft bifurcation without increase in aneurysm size.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Im: 000026/37
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A
ROYAL VICTORIA
[redacted]
M[redacted]
Acc:
2000 Jun 07
Acq Tm: 09:38:44.999000
150 ML OMNIPAQUE
R
L
130.0 kV
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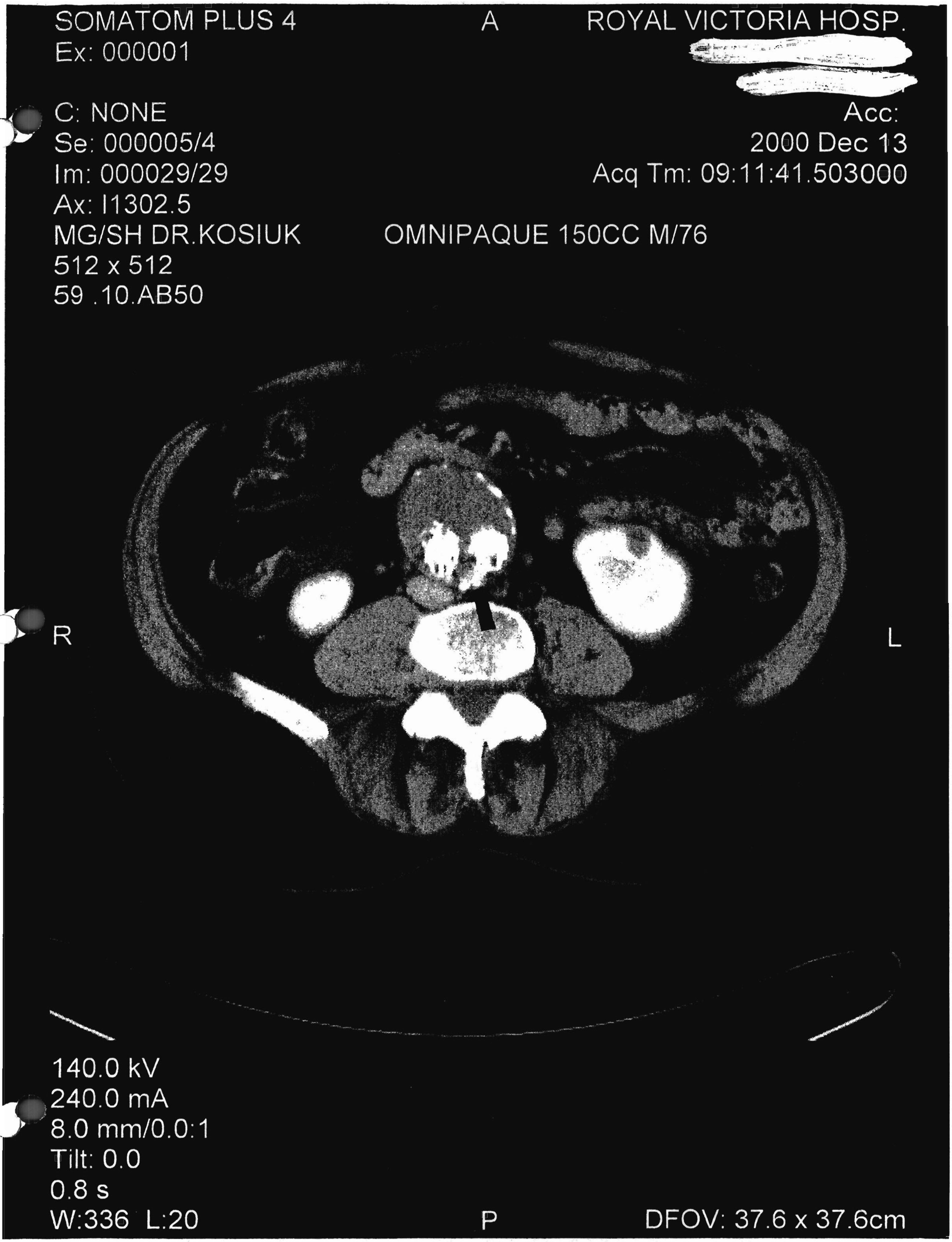
1.9 s
W:334 L:35
P
DFOV: 34.7 x 34.7cm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MG/SH DR.KOSIUK
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R
L
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240.0 mA
8.0 mm/0.0:1
Tilt: 0.0
0.8 s
W:336 L:20
P
DFOV: 37.6 x 37.6cm

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