CT Urography

Efforts to Reduce the Radiation Dose

PÅR DAHLMAN
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Abstract

Computed tomography urography (CTU) is today the imaging method used to investigate patients with suspected urinary tract malignancy, replacing the old imaging method intravenous pyelography (IVP) about a decade ago. The downside of this shift was that the effective radiation dose to the examined patient was eight times higher for CTU compared to IVP. Based on four different studies, the present thesis focused on efforts to reduce the CTU radiation dose.

In study I, the number of cysts and solid lesions in the separate scan phases was evaluated in 57 patients undergoing four-phase CTU 1997-98. The number of scans was reduced from four to three when the nephrographic scan was abolished following study I.

Study II registered the diameter of renal cell carcinoma (RCC) and the presenting symptoms in the total number of patients (n=232) diagnosed with RCC between 1997 and 2003. The results from study II showed that the critical size for RCCs to cause macroscopic hematuria was ≥4 cm. Study III was a dose-escalation study aimed to decide the minimal possible tube load in the unenhanced and excretory phase scans if the low dose images are reviewed together with normal dose corticomedullary phase images. Study III showed that it is possible to reduce the mean effective dose in three phase CTU from 16.2 mSv to 9.4 mSv with a combined low and normal dose CTU protocol. Study IV investigated the changes in the CTU protocol between 1997 and 2008, and the development of the effective radiation dose. Study IV clarified how the CTU protocol has changed between 1997 and 2008 and as a result the mean effective radiation dose to patients undergoing CTU in 2008 is only 39% of the effective dose in 1997.

In conclusion, the findings from the studies included in this thesis have contributed to a reduced radiation dose to patients undergoing CTU. The mean effective dose from CTU is at present only three times higher compared to that from the IVP.

Keywords: Urinary tract malignancy, renal cell carcinoma, urography, x-ray computed tomography, radiation dosage, dose escalation, hematuria/diagnosis

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“Lägg inte min son i grillen” Tomas Hansen

“Igen pappa! Igen!” glad 3-årig tjej som genomgått CT urografi och tyckte det var roligt att åka fram och tillbaka genom CT gantryt.

Dedication

To my three beloved girrls Karin, Inez and Isabella
List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.


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## Abbreviations

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<th>Description</th>
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<tr>
<td>ALARA</td>
<td>As low as reasonable achievable</td>
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<tr>
<td>ATCM</td>
<td>Automatic tube current modulation</td>
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<tr>
<td>BMI</td>
<td>Body mass index</td>
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<tr>
<td>CMP</td>
<td>Corticomedullary phase</td>
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<td>CT</td>
<td>Computed tomography</td>
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<tr>
<td>CTU</td>
<td>CT urography</td>
</tr>
<tr>
<td>CTDI&lt;sub&gt;vol&lt;/sub&gt;</td>
<td>Volume CT dose index (=weighted CTDI / pitch)</td>
</tr>
<tr>
<td>DLP</td>
<td>Dose length product (=CTDI&lt;sub&gt;vol&lt;/sub&gt; x scan length)</td>
</tr>
<tr>
<td>EP</td>
<td>Excretory phase</td>
</tr>
<tr>
<td>EU</td>
<td>Excretory urography</td>
</tr>
<tr>
<td>HU</td>
<td>Hounsfield units</td>
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<tr>
<td>i.v.</td>
<td>Intravenous</td>
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<tr>
<td>IVP</td>
<td>Intravenous pyelography</td>
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<td>IVU</td>
<td>Intravenous urography</td>
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<tr>
<td>IVP = IVU = EU</td>
<td></td>
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<tr>
<td>ICRP</td>
<td>International commission of radiation protection</td>
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<tr>
<td>LNT</td>
<td>Linear no threshold</td>
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<tr>
<td>MDCT</td>
<td>Multidetector row CT</td>
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<td>MR</td>
<td>Magnetic resonance</td>
</tr>
<tr>
<td>NP</td>
<td>Nephrographic phase</td>
</tr>
<tr>
<td>RCC</td>
<td>Renal cell carcinoma</td>
</tr>
<tr>
<td>SI</td>
<td>Systeme Internationale</td>
</tr>
<tr>
<td>TCC</td>
<td>Transitional cell carcinoma</td>
</tr>
<tr>
<td>UCC</td>
<td>Urothelial cell carcinoma, new name of TCC</td>
</tr>
<tr>
<td>US</td>
<td>Ultrasound</td>
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Introduction

X-rays have been in use 115 years. The experiences made by the early x-ray pioneers taught us that radiation is hazardous. The lack of knowledge of the dangers of ionizing radiation and unshielded x-ray tubes resulted in radiation burns, malignancies and deaths among early radiologists (1, 2). Present day radiologists are protected from the dangers of radiation by knowledge, improved technology and international and national radiation protection guidelines.

Presently due to technical improvements in computed tomography (CT) technology, the use of x-rays from CT is increasing (3). CT is a high dose technique compared to conventional x-rays and as CT replaces previous standard x-ray examinations and also new indications for CT scanning is emerging (4) there is increased concern that the radiation dose from CT to the entire population is increasing (3, 5).

Patients who undergo x-ray investigations, including CT, are subjected to low dose radiation. Although no conclusive evidence exists that low dose radiation is harmful, in theory also low dose radiation may cause DNA damage, potentially causing cancer or inheritable traits. All application of ionizing x-rays in diagnostic imaging must be done with caution. The benefits of the examination to the individual patient must outweigh the risks.

In uroradiology, the intravenous pyelography (IVP) has been replaced by CT urography (CTU) (Fig 1). CTU causes an increased radiation burden compared to IVP (Fig 2) and this increased radiation dose is justified by the better diagnostic capabilities of CT (6-10). However, the CTU protocol must always be optimized according to the ALARA principles (as low as reasonable achievable) (11). This thesis presents our efforts to optimize the CTU protocol in order to reduce the radiation dose to our patients.
The number of IVP and CTU examinations performed annually in Uppsala between 1992 to 2004 and the estimated future development. The CT examinations was performed on three different Siemens CT systems, Somatom Plus, Somatom Plus 4 and Sensation 16. The estimated effective dose from 3-phase CTU in 2004 was 13.5 mSv. The effective dose from IVP varied between 2.5 to 3.5 mSv. The predictions made in this study, presented at ESUR 2005 (“Is the radiation dose increasing in uroradiology?”, Dahlman P, Jangland L, Magnusson A., presented at ESUR 2005, Ljubljana, Slovenia) proved to be quite accurate as the last IVP laboratory was replaced by a CT scanner in 2007.
Figure 2:
When multiplying the workload statistics in Fig 1 with the mean effective dose from the different examination protocols used the total effective dose was calculated. The study presented at ESUR 2005 (“Is the radiation dose increasing in uroradiology?”, Dahlman P, et al, presented at ESUR 2005) showed clearly that the shift to CTU would result in a sharp increase of the collective radiation dose, especially if the radiation dose from CTU would remain unchanged.
Background

Uroradiology

The urinary tract is a vital organ system and physicians in ancient Babylonia, India, and Greece diagnosed disease in the urinary tract and elsewhere in the body by inspecting, smelling and tasting urine (12). A few of these diagnostic methods have survived and are used also in modern medicine. In addition, the last century has provided new diagnostic tools for physicians to diagnose disease in the urinary tract.

Uroradiology was born within a year following Wilhelm Conrad Röntgens discovery of x-rays 1895. The first application was detection of urinary tract calculi and following the discovery of various contrast materials that could be installed into the urinary tract, new applications were introduced, cystography in 1903, and retrograde pyelography in 1906. The first article describing visualization of the renal collecting system by intravenous administration of iodine was published in 1923 and in 1929 intravenous urography (IVP) was established (13). Now, both the collecting system and the renal parenchyma could be studied.

The following 45 years, the IVP was the most important uroradiological examination (Fig 3). In the 1970s several cross sectional imaging techniques challenged the IVP. Ultrasound (US), computed tomography (CT) and magnetic resonance tomography (MR) all provided excellent visualization of the renal parenchyma. The intravenous urography however was well up to the challenge as it was still best at visualizing pathology in the collecting system and had advantages to ultrasound and MRI in detecting calculi.

CT is since the late 1980s and 90s widely used in radiologic evaluation of the kidneys and urinary collecting system, including renal masses (6, 7), infection (8), trauma (9), and urinary calculi (10). Improvements in CT technology facilitating faster single breath-hold scanning have since the late 1990s resulted that CT is commonly used instead of IVP for evaluation of the above mentioned clinical problems. Later studies have proved CT as good as IVP in detecting pathology in the collecting system (14, 15). CT has however one disadvantage to the IVP and that is the higher radiation dose.
Figure 3:

a-d: Images before contrast administration. These images are used to detect urinary tract calculi.

e: Tomography image, used to locate the level of the kidneys.

f: Repeated tomography image, acquired directly following i.v. contrast injection. In this image the renal contour is visualized.

g-i: Following image f. an abdominal compression device is applied in order to achieve distended and opacified renal collecting systems. Approximately 5-10 minutes later, three images of the contrast filled renal collecting systems and pelvises are acquired - one image straight on and two oblique. In these images one look for filling defects suggesting possible
UCC. Images f. and g-i are important to evaluate if renal stasis is present, does the kidneys bilaterally enhance and excrete i.v. contrast.

j: Then the compression device is released and an image of the whole urinary tract is acquired.

k: Image focused over the bladder and the distal ureters.

l: Last image with the patient turned into prone position, focus over the whole urinary tract. Then the radiologist looked through the images before the patient left the examination room. Fairly often extra images were needed, for example having the patient void and then acquire new images over the bladder to visualise the distal ureters better.
Hazards of x-rays

Following the discovery of x-rays in 1895 the technique spread rapidly and was within months practiced by scientists and physicians worldwide. Already in 1896 reports were published on severe x-ray induced dermatitis. Reports published 1911-14 identified 198 cases of x-ray induced malignancy and 54 deaths among radiographers (2). A radiation protection pioneer was William Rollins, a dentist, who in the early 1900s urged radiologists to use only the smallest x-ray exposure necessary. Rollins made several important contributions: enclosing the x-ray tube to protect radiologists and patients, shutters, rectangular collimation, selective filters to screen out unwanted low quality radiation. Most x-ray operators ignored the early warnings of the hazards of x-rays. The radiation protection efforts presented by Rollins were decades ahead of his time. In 1915 the British Roentgen Society published the first radiation protection guide “Recommendations for the protection of X-ray operators” and in 1928 at the second international congress of radiology held in Stockholm, the international commission on radiation protection (ICRP) was formed. Since then the ICRP issues guidelines on radiation protection, which are the basis of international and national laws and regulations (16).

In 1956 Warren (17) reported that US Radiologists between 1934-39 lived until 56 compared to other specialities life span of 62 years. In another study (18) the authors showed that the difference in life span was only seen for radiologists who started their career prior to 1921. Before World War II new radiation protection measures were implemented and improved x-ray tubes facilitated shorter examination times. These changes protected radiologists from the radiation damages of the x-ray pioneers.

The upper dose limits suggested by modern radiation protection guide-lines are conservatively determined and the radiation doses received by patients are low and constitute a negligible risk of injury. Later atomic bombs and nuclear power has been in the focus of attention and the radiation protection efforts have shifted to protect the entire population. It is known that high dose radiation is harmful but there have since the 1960s been need of large studies to prove that also low dose (<100mSv) radiation is harmful. The atomic bomb survivors in Japan have been extensively studied and in the approximately 80 000 survivors, 400 excess cancer deaths have been registered (19). Forty percent of the exposed cohort is still alive and further follow up will hopefully provide increased knowledge of the long-term effect of radiation (20). The issue is not yet settled and there is still a debate among researchers if low dose radiation is dangerous or not. Is there a linear correlation between radiation dose and its harmful effects or is there a threshold level below which radiation is not harmful? The supporters of the hormesis theory claim that low doses of radiation may even be healthy due to stimulation of the immune system (21).
**X-rays**

X-rays are radiant energy similar to light. The difference is that x-rays with a shorter wavelength contain higher energy and which enables them to penetrate the human body. The x-rays are produced from an x-ray tube (Fig 4), a vacuum tube with a cathode emitting electrons and an anode collecting them, producing an electrical current. A high voltage source accelerates the electrons leaving the cathode. When the electrons hit the metal anode x-rays are created.

![X-ray Tube Diagram](image)

**Figure 4:**
Illustration - x-ray tube. Electrons are emitted into a vacuum tube from the cathode and collected by the anode, creating an electrical current. When the electrons connect with the anode, x-rays are created.

The x-ray tube is very inefficient and 99% of the energy is lost in heat and useless non-penetrable low energy, x-rays. In opposite to the first x-ray tubes modern x-ray tubes are shielded to protect the tube operator and the patient from unwanted low-energy and scattered x-rays. Only x-rays going straight towards and through the patient are wanted. Therefore collimators stop x-rays going in unwanted directions before they reach the patient. In order to shield the patient from the low-energy x-rays a thin metal filter is applied between the x-ray tube and the patient to stop low-energy x-rays. To minimize the number of x-rays needed to create an image a grid is used to stop scattered, non-straight going x-rays before reaching the image detector.
Basic CT technology

The CT scanner can be described as an x-ray tube and an x-ray detector that rotates around the patient and almost continually sends a fan shaped beam x-rays through the patient (Fig 5). The computer then calculates images from the collected attenuation data (Fig 5 and 6). In contrast to conventional radiographs CT images are free of superimposing structures as each image represents a cross-sectional slice through the patient. Early CT scanners required long scan times and the images had poor resolution. Manufacturers have since sought shorter examination times, higher image resolution and faster computer reconstruction times.

Figure 5:
Schematic drawing of single slice- and multidetector row CT. The patient is in supine position and move in single slice CT stepwise through the CT gantry and in multidetector row CT continually through the gantry. The x-ray tube and the detector rotate around the patient.

Dose estimations in CT

The most used index today for measuring the dose from MDCT equipment is the CTDI$_{vol}$*. The DLP (dose length product) is the CTDI$_{vol}$ multiplied by the scan

*The CT dose index (CTDI) represents the radiation dose of a single axial CT slice and is determined using acrylic phantoms. The most commonly cited index for modern multidetector row CT scanners is the CTDI$_{vol}$. It is calculated by dividing the CTDIw (reflects the weighted sum of two thirds peripheral dose and one third central dose in a acrylic phantom) with the pitch.
length (slice thickness × number of slices). There are conversion factors to estimate the corresponding effective dose (22). To decide the effective dose more accurately, individual organ doses must be determined and then the effective dose is the sum of the organ doses multiplied by the corresponding weighting factor (23).
CT history

Following the introduction of CT in the early 1970s a rapid technical development began. CT was considered one of the great inventions in medicine and was awarded the Nobel Price in 1979. In the 1980s technical development was slower and concurrent advances in MR and US lead to the opinion that CT was dead (4) and soon to be replaced by MR. Then spiral CT was introduced in 1989 and focus shifted back to CT in the 1990s. The technical development has since continued, scan times have shortened and image resolution improved. CT re-appeared as a key imaging modality and was rapidly integrated into clinical practice. The technical development continued in the 2000s with the 16-slice scanner in 2001 (Fig 7 A and B), the 64-slice scanner in 2004, dual source scanner in 2005 (Siemens Somatom Definition), the 256 (Philips Healthcare’s Brilliance iCT) and 320-slice scanners in 2007 (Toshiba Medical Systems, Aquilion ONE) and the dual source 128-slice scanner in 2009 (Siemens Somatom Definition Flash). Now the “slice wars” is said to be over and the vendors instead focus on dose reduction (“dose wars”) (24) by improving dose modulation techniques, making hardware improvements such as adding additional beam filters, improving detector dose efficiency, developing scanning protocols that do not overlap excessively, and developing reconstruction algorithms that can handle lower tube current.

The early CT scanners used single slice technique where the patient moved step-wise through the CT gantry. Each step through the CT gantry represented a CT slice/image. The first body CT scanner in Uppsala needed 18 seconds for each slice, the slice thickness was 8 mm and with an interval of 8 mm in between slices, 8 minutes was needed to scan 45 cm (Magnusson A., personal communication).

Modern CT scanners use spiral multidetector technique where the patient continually moves through the CT gantry, scanning through large volumes of the patient in seconds. A 128-slice scanner covers 60 cm (thorax/abdomen) in 2.5 seconds and the Siemens dual source Flash scanner in 2 seconds.
CT dose reduction

With the increased use of MDCT in the early 2000s focus also turned to the radiation dose. The fact that children undergoing CT might be at risk for developing future malignancies got media attention following a series of articles in the American Journal of Roentgenology in 2001 (25, 26).

CT parameters in pediatric patients were previously set the same as adults leading to unnecessary high radiation doses. This as a higher radiation dose is needed to get the wanted image quality in large patients compared to normal- or small size patients. The simplest parameter to change in order to reduce the radiation dose is the tube current. The relationship between tube current and radiation dose is linear, decreasing tube current by 50% will decrease radiation dose by 50%.

The development of individual scan protocols soon followed and dedicated pediatric protocols. This reduced radiation doses also to adult patients. Previously also all adult patients were examined with CT settings that would render acceptable image quality in all patients - including obese patients. Instead of standard protocols for all patients with varying image quality, the aim was to have constant noise in the images by adjusting the tube current (mAs-value) in relation to patient size. As the mAs settings were adjusted to patient size, the radiation dose to small and normal size patients was reduced. The manufacturers realized that they must address the dose issue and lately several technological innovations that promise to decrease the radiation have been introduced (27). Below are a few examples of such technical innovations.

X-ray beam utilization

Focal spot tracking: Improved techniques to control x-ray tube focal spot motion and beam collimation, enhances scanner efficiency (overbeaming is reduced as the beam is stabilized on the detectors allowing an x-ray exposure profile that is narrower than the detected x-ray profile, and the radiation dose associated with multidetector row CT is reduced) (27).

X-ray filtration

X-ray filters selectively remove low energy x-rays and thus decrease absorbed radiation. A dose reduction of 15% has been reported with updated filters. Bow-tie filters or beam-shaping filters can reduce the surface radiation dose by 50% by further reducing the lower energy x-rays in fan shaped x-ray beams (27).
Figure 7A - CT examination from 1991:
Renal CT examination performed in 1991. The multiphase CT examination depicts the kidneys in unenhanced, nephrographic and excretory phase. The examination consists of 36 axial images. Due to the slow scan time the CT examination must focus on the kidneys. The kidneys were only scanned twice, pre- and post i.v. contrast.
Figure 7 B - CT examination from 2005:
A CTU performed in 2005 consists of more than 2000 images. The whole abdomen is examined from the diaphragm to the pubic symphysis. The 16-slice scanner provides isotropic imaging with 3D multiplanar reformats.

1 a + b: Unenhanced phase images through the kidneys in coronal and axial planes.
2 a + b: Corticomedullary phase images. The images are acquired 20-30 sec following the start of i.v. contrast injection. The contrast is still in the arteries and the renal cortex but has also passed through the kidney and into the renal vein.
3 a + b: Excretory phase images. Five minutes following contrast injection, the contrast has passed through the kidneys to the renal pelvis, ureters and the bladder.

Patients ingest 800 ml of water prior to the examination and are told not to void. In addition they receive 10 mg of diuretics at the start of the examination. These maneuvers are performed to improve distension and the contrast opacification in the excretory system and thereby improve UCC detection.

UP= unenhanced phase, CMP= corticomedullary phase, EP= excretory phase.
**Automatic modulation of tube current (ATCM)**

ATCM can substantially reduce radiation dose. The concept is based on the premise that pixel noise on a CT scan is attributable to noise in the projections. By adjusting the tube current to patient anatomy, i.e. increasing the tube load in the more dense areas such as the shoulder area and further scanning with a higher tube load in the coronal direction compared to the anteroposterior direction. A desired noise level can be maintained and thereby improve dose efficiency. In Siemens the ATCM techniques are called CARE Dose* and CARE Dose4D**.

**Filters**

Radiation dose reduction is limited by increased image noise. Different techniques have been developed to decrease image noise in scans with reduced dose. The most used technique has been called fan shaped filtered back projection, a smoothing algorithm which decrease noise on low-dose CT images but also decrease lesion contrast and conspicuity (27). As computer performance improve, new iterative reconstruction algorithms have been introduced (GE call their product ASIR) (30). This algorithm is considered a compromise to the more complex iterative algorithms, model-based iterative reconstruction (MBIR). MBIR improve image quality significantly but require to much computer power and therefore impractical for clinical use. The ASIR technique is expected to be able to reduce the dose by 30-50%.

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* CARE Dose (Siemens Medical Systems, Forchheim, Germany) is an attenuation-based on-line modulation in the x-y direction of the tube current. The attenuation data from previous rotations are analyzed in real time to determine optimal tube current for each projection angle in the next rotation (28).

** CARE Dose4D (Siemens Medical Systems, Forchheim, Germany) is an automatic exposure control by which the tube current is adapted to the attenuation properties of the patient in the x-y and z directions. In the x-y direction, the tube current is adapted, as with CARE Dose. In the z direction, the modulation of the tube current is based on attenuation data from the topogram (scout view)(29). The adaptation is in the Uppsala CTU protocol set as “weak” for slim patients and “average” for obese patients. Quality reference mAs is specified in the scan protocol and refers to the effective mAs for the required image quality in a patient of standard size. With CARE Dose4D, the actual effective mAs increases (compared to the quality reference mAs) if the patient is large and decreases if the patient is small.
Projection-adaptive reconstruction filters

Projection space filters increase the filtration of signal-dependent noise in the reconstruction data and thus minimize the loss of resolution in areas with loss of signal (for example the shoulders). The use of these filters result in loss of image resolution (less than 5%). However the use of projection-adaptive reconstruction filters permit imaging at lower dose settings (27).

Shutters – prevent z – overscanning (= overranging)

A less known potential source of extra radiation is “overranging”. In abdominal scanning a 16 slice MDCT overranges between 3.2 and 5.2 cm (31, 32). The study by van der Molen (31) investigated different 16 slice MDCT scanners, the authors predicted that the z overscanning effect is more pronounced in scanners with wider detector rows. The vendors now offer MDCT scanners with automatic shutters that shield patients from extra irradiation caused by z overscanning.

The overranging is dependent of the reconstruction algorithms used to calculate images. In the Siemens Sensation 16 scanner the overranging depend on the selection of parameters that are prospectively selected (van der Molen A., personal communication). If the scanner prospectively will use 1 mm thin slice data, the resulting overrange will be according to the slice width (SW) 1 mm. However if the scanner will be prescribed to reconstruct both 1 mm and 5 mm images the overranging will be 1 SW = 5 mm. This because in the Sensation 16, 5-10 mm SW images are done with a different reconstruction algorithm (faster, more overrange) than the 1-4 mm SW algorithm. This can be seen on the scanner. If one scan prospectively only 1 mm SW from position 0 to position 420 it will result in 420 + 1 mm = 421 mm in slices, later reconstruction to 5 mm will return 420/5 = 84 images. However if one scan prospectively 1 mm and 5 mm from position 0 to 420 it will result in 420 + 5 mm = 425 mm in slices. Later reconstruction to 5 mm will produce 425/5 = 85 images. This means the overrange increase 4 mm.

Image reconstruction algorithms – less x-rays needed to create CT images.

New reconstruction algorithms are developed, algorithms that can handle lower tube current, creating the possibility to image with lower radiation doses (27).
Radiation – relevant terms

Radiation
In physics, any process in which energy emitted by one body travels through a medium or through space, ultimately to be absorbed by another body.

Ionizing radiation
Ionizing radiation consists of subatomic particles or electromagnetic waves that are energetic enough to detach electrons from atoms or molecules, ionizing them. This can disturb biological tissues, and can cause mutations and cancer.

Absorbed dose
The amount of damage done (especially to living tissue) by ionizing radiation is closely related to the amount of energy deposited. This is called the absorbed dose. The SI unit of absorbed dose is gray (Gy), with units J/kg, and represents the amount of radiation required to deposit 1 joule of energy in 1 kilogram of any kind of matter.

Equivalent dose
Equal doses of different types of radiation cause different amounts of damage to living tissue. Therefore the equivalent dose was defined to give an approximate measure of the biological effect of different types of radiation, for example, 1 Gy of alpha radiation causes about 20 times as much damage as 1 Gy of x-rays. The sievert (Sv), with units J/kg, is the SI unit of equivalent dose.

Radiation weighting factor ($W_r$)
Equivalent dose is calculated by multiplying the absorbed dose by a weighting factor ($W_r$) that varies for different types of radiation. X-rays have $W_r = 1$.

Tissue weighting factor ($W_T$)
The tissue weighting factor ($W_T$) which compare the susceptibility of the different organs (Table 1) (22).

Justification
To determine that a planned x-ray examination is, overall, beneficial, i.e. whether the benefits to the individuals and the society from introducing or continuing the examination outweigh the harm (including radiation detriment) resulting from the activity.

Optimization
In imaging to adapt the acquisition parameters as low as reasonable achievable. To find the balance between the diagnostic needs, acceptable image quality and the well-being and future risk of the patient.
Recommended tissue weighting factors.

<table>
<thead>
<tr>
<th>Tissue</th>
<th>( W_T )</th>
<th>( \Sigma W_T )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone-marrow (red), Colon, Lung, Stomach,</td>
<td>0.12</td>
<td>0.72</td>
</tr>
<tr>
<td>Breast, Remainder tissues*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gonads</td>
<td>0.08</td>
<td>0.08</td>
</tr>
<tr>
<td>Bladder, Oesophagus, Liver, Thyroid</td>
<td>0.04</td>
<td>0.16</td>
</tr>
<tr>
<td>Bone surface, Brain, Salivary glands, Skin</td>
<td>0.01</td>
<td>0.04</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>1.00</td>
</tr>
</tbody>
</table>

* Remainder tissues: Adrenals, Extrathoracic (ET) region, Gallbladder, Heart, Kidneys, Lymphatic nodes, Muscle, Oral mucosa, Pancreas, Prostate (♂), Small intestine, Spleen, Thymus, Uterus/cervix (♀).

Table 1:
Organ dose weighting factors:
The total weighting factor for the whole body is 1. One Gy of radiation delivered to the whole body is equal to one sievert (for photons with \( W_T = 1 \)). Therefore, adding the weighting factors for each organ create the sum 1. From ICRP 103.

**Effective dose**
The effective dose is found by calculating a weighted average of the equivalent dose to different body tissues/organs, with the weighting factors designed to reflect the radiosensitivities of the different tissues.

**Damage caused by ionizing radiation - deterministic effects**
These injuries are not subject to chance and the radiation causes wide spread cell death and organs / tissues cease to function. High radiation doses are required; following an acute whole body dose of 7-10 Gy the chance of survival is low. Following an acute whole body dose of 3-5 Gy 50% of patients would die within 60 days. Following radiation to limited parts of the body higher radiation doses can be tolerated.

**Damage caused by ionizing radiation - non-deterministic effects**
Stochastic effects occur by chance and occur late following the radiation exposure. The radiation itself did not cause the cancer, instead damage to the DNA and an increased risk of later developing cancer. According to radiation guidelines the effect has no threshold and the chances of seeing the effect increase with the dose (22).
Hazards of low dose radiation

There is no consensus on the dangers of low-dose radiation (Fig 8). Recent reports published in high impact scientific journals (5) claim that the increased use of CT in modern medicine cause and will cause an increased rate of malignancies and cause 2% of all deaths in cancer in the US. Tubiana et al argue against the linear no threshold (LNT) theory and claim that low dose radiation is not harmful or may even be beneficial (33). The authors continue that the exaggerated hazards of low dose radiation cause public fears that scare the general public, “fear of radiation can cause more harm than radiation itself”. Following the Tjernobyl accident in 1986 several tens of thousands of women in Europe performed unnecessary abortions due to fear of damaged fetuses. Similarly breast cancers might go undetected because women’s irrational fear of the carcinogenic effect from Mammography.

Although the debate on the LNT theory continues and no definite proof exist of the hazards of low dose radiation, each CT examination must be justified and overuse of CT must be avoided. In individuals more at risk for radiation (26, 34), young individuals and women, alternative non-ionizing methods such as MR or US should be considered. A recent article in the US even suggests that informed consent on the radiation risk must be obtained before each examination involving ionizing radiation (35).

Even if a CT examination is justified the CT scan must still be optimized. This means that the radiation dose from CT protocol must be as low as possible without losing clinically important information.

Difference in radiation dose from IVP and CTU

In uroradiology the method of choice to examine patients with suspected urinary tract malignancy has changed from IVP to CTU. Previously patients were first screened with an IVP and then in all cases with suspected malignancy and most cases with other pathology follow up examinations with CT or US were performed to confirm the findings of the IVP.

In the late 1990s when the research presented in this thesis started a CTU in Uppsala consisted of a four phase CTU protocol and the radiation dose from a CTU was 8 times higher then from an IVP, close to 30 mSv from CTU compared to 3.5 mSv from an IVP.
Figure 8:
At the 250 - 500 mSv level detrimental effects are known (23). Two different theories on the hazards of low dose radiation; ①. The linear no threshold theory. ②. The risk drops off to zero at some level. Until more definite data exist one must assume that there are no level under which low dose radiation does not cause an increased risk of malignancy.
Aim of the thesis

Overall aim

The overall aim of the thesis was to evaluate the CTU protocol with a focus on radiation dose and to optimize the protocol in order to reduce the radiation dose.

Specific aims of the individual studies

Paper I

To evaluate how many renal lesions that can be detected in the different phases of contrast enhancement in a four phase CTU. A further aim was to evaluate in which phase solid renal lesions were best detected and characterized and if any phase could be excluded without loss of important information. It was also investigated during which phase the renal veins and the caval vein were best visualized.

Paper II

To investigate the size of renal cell carcinomas (RCC) when they cause macroscopic hematuria or other symptoms and/or signs suggesting an upper urinary tract malignancy.

Paper III

To investigate how far it is possible to reduce the radiation dose from CTU by reducing the reference eff. mAs in the unenhanced- and excretory phase when systematically evaluating low dose unenhanced phase and excretory phase images together with normal tube load corticomedullary phase images.

Paper IV

To examine the changes in the CTU protocol between the years 1997 and 2008, and how these changes have influenced the effective radiation dose.
Material and methods

Patients

Paper I
In paper I, sixty patients, age 61±14 (min 21, max 84) years, referred for a standard four-phase CTU were enrolled between September 1997 and August 1998. Three patients were excluded. Two patients because image evaluation was impossible, one patient with a large haematoma and other postoperative changes and one patient with advanced cystic kidney. The third patient was excluded due to extravasation of the contrast medium. At the time no ethics committee approval was needed as all patient information was handled anonymously.

Paper II
In paper II, a retrospective review was performed to find all patients diagnosed with RCC at Akademiska Sjukhuset between 1996 to 2003. Two hundred and thirty-two patients were identified, age 68±11 (min 40, max 90) years, 136 males and 96 females. At the time no ethics committee approval was needed as all patient information was handled anonymously.

Paper III
In paper III, twenty-seven patients age 74±9 (min 56, max 89) years; BMI 25±3 (18-28) kg/m², 20 ♂, 7 ♀) referred for CTU were enrolled. The faculty ethical review board approved the study. Written and informed consent was obtained from all patients. Only patients older than 45 years and with a Body Mass Index (BMI) < 30 kg/m² were eligible for the study.

Paper IV
In paper IV, the study was based on a total of 102 patients undergoing CTU due to suspected urinary tract malignancy (72 males, age 66.8±14.6 (min 32, max 89) years and 30 females age 64.4±15.2 (min 31, max 89) years). The patients were divided into five groups; group A-E, representing the different versions of the CTU protocol that was in use between 1997 and 2008.

The study population consisted of five different groups of patients: groups A (n=38), B (n=38), C (n=38), D (n=27), and E (n=37). In 2005 and 2008, patients were examined using ATCM, and the mAs values were unique to each patient.

In accordance with the prevailing ethical rules in 1997, 1999, and 2001, no ethics committee approval was needed, as all patient information was handled anonymously. Ethical approval was received in 2005 and 2008.
Methods

Paper I

The patients underwent a standard four-phase CTU. The CTU was performed on a Somatom Plus 4 (Siemens, Forchheim, Germany) with acquisition parameters: tube voltage 120 kV, tube load 210 mAs, slice collimation 5 mm, table speed 7.5 mm/rotation, rotation time 0.75 s, increment 5 mm. Contrast material used was Iobitridol 300 mg I/ml (Xenetix, Laboratoire Guerbet) or Iopromide 300 mg I/ml (Ultravist, Schering). A dose of 1.5 ml/kg bodyweight was administered at a rate of 3-4 ml/s by an automatic injector (Ulrich CT Injector XD5500, Ulrich Medizintechnik, Ulm, Germany). Directly following the contrast material infusion, 40 ml physiological saline was injected at an unchanged injection rate.

The UP scan was performed first. Then the CMP scan followed with a delay of approximately 30 s after the start of the i.v. contrast material injection. The start of the CMP scan was controlled by the care bolus system, the scan commencing when the enhancement of the abdominal aorta exceeded 150 HU. The NP scan started 60 s after the start of the CMP scan and the EP scan 5 min after the start of the CMP scan.

Every contrast phase was reviewed separately and size (mm), attenuation (HU), characteristics (cyst/solid) and location (cortex/marrow/sinus) of all detected renal lesions were registered. For solid lesions, the confidence in characterization of was graded in each contrast phase. In each scan phase the ability to exclude tumor thrombus was judged.

Paper II

The diagnostic database of Akademiska sjukhuset were searched to find all patients diagnosed with RCC between 1996 and 2003. The clinical notes and relevant imaging examinations were studied. Patients were then grouped according to the presenting symptoms and/or signs; Group A incidental RCCs (i.e. tumors that presented without symptoms and/or signs suggestive of RCC), Groups B-E consisted of patients with symptoms and/or signs suggestive of RCC. Where group B - macroscopic hematuria, group C - local symptoms from the kidney, group D - symptoms caused by metastasis and group E - paraneoplastic symptoms.

All patients underwent CT. One-hundred and seventy-seven patients at Akademiska sjukhuset, with four different CT systems: Somatom Plus, Somatom Plus 4, Volume Zoom and Sensation 16 (all from Siemens, Forchheim, Germany). Remain-
ing 55 patients underwent CT examination at outside hospitals. Several different
CT protocols were employed. The slice thickness varied between 1 mm (increment
1 mm) and 10 mm (increment 10 mm). Most examinations used a 3 - 5 mm slice
thickness with a corresponding increment between images. Sixty-seven percent of
the patients underwent CT urography consisting of three or four scan phases: UP,
EP, CMP and/or NP scans. The remaining patients underwent standard contrast-
enhanced CT abdomen examinations, which were not focused solely on the urinary
tract. I.v. contrast was not administered in 2% of the examinations. Tumor size was
measured from CT images in three dimensions on a workstation (Impacs; Agfa,
Waterloo, Ont., Canada).

**Paper III**

The patients were examined with Siemens Sensation 16, acquisition parameters:
120kV, rotation time 0.5 s, collimation 0.75, slice thickness 5 mm, increment 5, pitch
1, reference effective mAs - 100/120/100 (=UP/CMP/EP). The examinations were
performed with ATCM in the x-y-axis (CARE Dose, Siemens Medical Systems,
Forchheim, Germany). The standard three phase CTU consisted UP-, CMP- and EP
scans. All scans were performed from the diaphragm to the pubic symphysis.

In order to distend the collecting system and the bladder, the patients received oral
hydration with 800 ml water during 120 minutes prior to the exam, and were told not
to void. Furosemide (10 mg i.v.) was injected at the start of the examination. Eighty
ml of iopromide 300 mg I/ml (Ultravist; Bayer Schering Pharma, Berlin, Germany)
was then administered at a rate of 3-4 ml/s with an automatic injector (Stellant D,
Medrad Inc, Indianola, Pa., USA). CARE bolus was used and the CMP scan started
automatically when the attenuation value in the aorta at the level of the diaphragm
reached 200 HU. EP scan was performed with a 5-min delay.

The included patients underwent in addition to the standard CTU, extra low dose
scans in the unenhanced and excretory phase according to a decided dose escalation
protocol. In the EP, patients were randomized if low- or normal mAs scans were to
be performed first.

The additional low dose scans in UP and EP were performed one of the four
decided dose levels, starting at the 20 eff. mAs level, with the following reference
tube loads: 20 eff. mAs (CTDIvol 1.7 mGy), 40 eff. mAs (CTDIvol 3.3 mGy), 60
eff. mAs (CTDIvol 5.0 mGy), 80 eff. mAs (CTDIvol 6.6 mGy). CMP scans were
always performed with a tube load of 120 eff. mAs (CTDIvol 9.9 mGy). The included
patients also underwent standard dose scans in UP and EP at 100 eff. mAs (CTDIvol
8.3 mGy). The patients were thereby their own controls. One patient was recruited
to at each dose tier at a time. The efficacy data was reviewed after every completed patient. The study advanced to the next dose tier if important information was lost in three patients.

**Image evaluation**

Image quality in low- and normal mAs images was further evaluated measuring attenuation and noise, expressed as the standard deviation (SD) of the Hounsfield Units (HU) using standardized regions of interest (ROI’s) in the liver in low- and normal dose images. Attenuation and image noise measurements were further performed in all focal renal lesions. Artifacts observed in the low dose images were judged on a 5-point scale (1 = no artifacts, 2 = slight artifacts, 3 = moderate degree of artifacts, 4 = heavy artifacts making diagnosis difficult, 5 = non-diagnostic due to artifacts).

The low dose images were judged according to a modified version of the European Commission of image quality criteria (37) for delineation of anatomic structures and presence of urinary tract pathology. Second, the standard dose images were judged in the same way and third, the low mAs images were evaluated together with the CMP images to see if any shortcomings of the low mAs images was nullified. The diagnostic confidence was scored after viewing each step: 1. the low mAs images, 2. normal mAs images and 3. Low mAs images together with normal dose CMP images and diagnostic confidence (on a 1-5 scale; where 1 = non-diagnostic, 2 = poor, 3 = acceptable, 4 = good, 5 = excellent).

In case of discrepancy between the low- and normal dose images, and the error was not corrected after reviewing the low dose images together with CMP images, then the examination was judged a failure. A dose tier was abandoned after three examinations failures.

**Effective Dose**

The effective dose (E) to the standard patient was calculated with the ImPACT CT Patient Dosimetry Calculator (version 1.0.2; ImPACT, London, U.K.). In the program, start of the operator-planned scan was set to the diaphragm in the virtual patient (position 44), and end of the scan was set to the pubic symphysis (position 2). Planned scanning length was thus set at 42.0 cm per phase. An additional average overrange of 3.0 cm per phase (1.5 cm on each side) was incorporated in the dose calculations, increasing the scanrange range from position 45.5 to position 0.5. Angular automatic tube current modulation was used in the XY-plane. Therefore, the effective mAs varied between patients. The mean value of the effective mAs in each phase was used in the calculations.
Paper IV

Two different Siemens CT scanners (Forchheim, Germany) were used: a Somatom Plus 4, for the groups studied in 1997, 1999, and 2001, and a Sensation 16, for the groups studied in 2005 and 2008.

In 1997 to 2001, 100 ml of iopromide (300 mg I/ml, Ultravist; Bayer Schering Pharma, Berlin, Germany) was injected intravenously at a rate of 3-4 ml/s with an automatic injector (Ulrich CT Injector XD5500; Ulrich Medizintechnik, Ulm, Germany). A care bolus system (CARE Bolus; Siemens, Erlangen, Germany) automatically started the CMP scan when the enhancement of the abdominal aorta exceeded 150 HU. Each patient received 10 mg of furosemide intravenously administered on the CT table at the start of the CT examination.

In 2005 and 2008 the patients received oral hydration in order to distend the collecting system and the bladder and were told not to void prior to the CT examination. Eighty ml of iopromide (300 mg I/ml) was then administered at a rate of 3-4 ml/s with an automatic injector (Stellant dual-flow; Medrad Inc, Indianola, Pa., USA). CARE bolus was used and the CMP scan started automatically when the attenuation value in the aorta at the level of the diaphragm reached 200 HU. EP scan was performed with a 5-min delay.

Scanning parameters 1997 to 2008 are presented below.

Group A

Four phase CTU: UP, CMP, NP, and 5-min-delay EP scans. All scans except the CMP were performed from the top of the kidney to the pubic symphysis and the CMP scan included only the kidneys. Scanning parameters: 120 kV, 280 mAs, rotation time 0.75 s, pitch 1.5, slice thickness 5 mm, increment 5 mm.

Group B

Three phase CTU: UP, CMP, and 5-min-delay EP scans. All scans were performed from the top of the kidney to the pubic symphysis. Scanning parameters: 120 kV, 280 mAs, rotation time 0.75 s, pitch 1.5, slice thickness 5 mm, increment 5 mm.

Group C

Three phase CTU: UP, CMP, and 5-min-delay EP scans. All scans performed from the top of the kidney to the pubic symphysis. The patients were divided by the CT technician according to size, as “thin”, “intermediate”, and “large”, corresponding to tube settings of 100, 135, and 165 mAs. All patients in group C were intermediate size. Scanning parameters: 120 kV, 180mA (normal size patients – equals 135mAs), rotation time 0.75 s, pitch 1.5, slice thickness 5 mm, increment 5 mm.
**Group D**

Three phase CTU: UP, CMP, and 5-min-delay EP scans. All scans performed from the top of the kidney to the pubic symphysis.

The tube current in each scan phase was adapted to the information needed from each scan phase. The tube current was reduced in the UP and EP scans. An ATCM system was introduced in group D, CARE Dose (Siemens Medical Systems, Forchheim, Germany). Scanning parameters: 120 kV, effective mAs (i.e., true mAs divided by the pitch) 100/120/100, rotation time 0.5 s, collimation 16x0.75 mm, pitch 1, image reconstruction with slice thickness and increment: axial 5/5 mm and 1/1 mm, coronal 5/5 mm.

**Group E**

Three phase CTU: UP, CMP, and 5-min-delay EP scans. All scans from the top of the kidney to the pubic symphysis. The quality reference mAs levels were adjusted following the introduction of CARE Dose4D (Siemens Medical Systems, Forchheim, Germany). Scanning parameters: 120 kV, quality reference mAs 60/120/80 (=UP/CMP/EP), rotation time 0.5 s, collimation 16x0.75 mm, pitch 1, image reconstruction with slice thickness and increment: axial 5/5 mm and 1/1 mm, coronal 5/5 mm.

The effective dose (E) to the standard patient was calculated with the ImPACT CT Patient Dosimetry Calculator (version 0.99x; ImPACT, London, U.K.). The start of the scan was set to the diaphragm in the virtual patient (position 45), and end of the scan was set to the pubic symphysis (position 5) with exception of the CMP in group A where the end of the scan was set to just below the kidney (position 25). In groups A, B, and C, the mAs value in each phase was fixed, since dose modulation was not available. In groups D and E, tube current modulation was in use and the effective mAs varied individually. The mean value of the effective mAs in each phase was used in the calculations.
Statistics

**Paper I, II and IV**

The results are presented as mean±SD (range). Statistical analysis was performed with Microsoft Office Excel (2003; Microsoft Corp, Redmond, Wash., USA).

**Paper III**

All 27 patients who were enrolled and underwent additional low dose scans completed the study. There were hence no differences between the intention to treat and the per-protocol population. The diagnostic confidence is presented as mean ± standard deviation (range). Comparison of the diagnostic confidence score acquired with the low doses and high doses was performed with the Wilcoxon rank-sum test. Also, the diagnostic confidence acquired when combing the low dose image with the CMP information was compared to the diagnostic confidence when only considering the high dose image by using the Wilcoxon rank-sum test. A p-value of 0.05 was considered significant. Bland & Altman plots (38) plots were used to compare the accuracy and level of agreement in the attenuation measurements in high and low dose images. All analyses were performed using R Software version 2.11 (R Foundation for Statistical Computing, Vienna, Austria).
Results

Paper I

A total of one hundred and fifty-three simple cysts and 17 solid lesions were found in 48/57 patients (Table 2). Three of the solid lesions had image characteristics as angiomyolipomas, twelve as renal parenchymal tumors and two were characterized as UCC. Tumor thrombi in the renal vein were diagnosed in two patients.

Most, and an equal number of simple cysts were detected in the NP and the EP scan. However, the NP was more sensitive for cortical cysts and the EP was superior in detecting sinus cysts. The main difference between the NP and EP scans and the earlier scans was the ability of the NP and EP scans to detect small medullar cysts.

All solid lesions were detected in all phases when they were viewed separately. The angiomyolipomas were best characterized in the unenhanced phase. With the exception for one poorly enhancing tumor and the angiomyolipomas, the solid lesions was best characterized in the CMP scan (Table 3). One of the collecting system tumors was best characterized in the CMP followed by the NP, the EP and the UP. The other collecting system mass, later re-diagnosed as renal tuberculosis, was best characterized in the EP.

The renal veins were best evaluated in the CMP followed by the NP, EP and UP. The caval vein was best evaluated in the NP followed by the EP, UP and CMP.

Table 2

<table>
<thead>
<tr>
<th>Detection rate, size and location of simple renal cysts</th>
<th>Native phase</th>
<th>Cortical phase</th>
<th>Nephrographic phase</th>
<th>Excretory phase</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of cysts, n and (%)</td>
<td>60 (39)</td>
<td>97 (63)</td>
<td>142 (93)</td>
<td>143 (93)</td>
<td>153</td>
</tr>
<tr>
<td>Average diameter and (range) of total cysts, mm</td>
<td>22±15 (6–83)</td>
<td>17±14 (2–82)</td>
<td>14±13 (2–78)</td>
<td>14±12 (2–79)</td>
<td></td>
</tr>
<tr>
<td>Cysts in renal cortex, n and (%)</td>
<td>41 (68)</td>
<td>60 (100)</td>
<td>60 (100)</td>
<td>50 (83)</td>
<td>60</td>
</tr>
<tr>
<td>Average diameter and (range) of cortical cysts, mm</td>
<td>20±16 (6–83)</td>
<td>15±15 (2–82)</td>
<td>14±14 (2–78)</td>
<td>18±16 (3–79)</td>
<td></td>
</tr>
<tr>
<td>Cysts in the renal marrow, n and (%)</td>
<td>11 (15)</td>
<td>29 (39)</td>
<td>74 (100)</td>
<td>74 (100)</td>
<td>74</td>
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<tr>
<td>Average diameter and (range) in marrow cysts, mm</td>
<td>17±7 (7–34)</td>
<td>15±8 (3–34)</td>
<td>11±10 (2–62)</td>
<td>10±7 (2–36)</td>
<td></td>
</tr>
<tr>
<td>Sinus cysts, n and (%)</td>
<td>8 (42)</td>
<td>8 (42)</td>
<td>8 (42)</td>
<td>19 (100)</td>
<td>19</td>
</tr>
<tr>
<td>Average diameter and (range) in sinus cysts, mm</td>
<td>33±14 (19–61)</td>
<td>35±12 (21–54)</td>
<td>34±12 (22–52)</td>
<td>21±11 (6–40)</td>
<td></td>
</tr>
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</table>
Table 3
Confidence in characterisation of 12 renal parenchymal tumours in the different phases of contrast medium enhancement

<table>
<thead>
<tr>
<th>Native phase</th>
<th>Cortical phase</th>
<th>Nephrographic phase</th>
<th>Excretory phase</th>
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<tbody>
<tr>
<td>++</td>
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</table>

+ renal lesion detected, ++ suspected solid lesion detected, ++++ solid lesion detected and characterised, ++++ solid lesion detected and characterised with confidence

Paper II

Between 1996 and 2003, two hundred and thirty-two patients were diagnosed with RCC. Of the 232 RCC, 67 (29%) were incidental (Group A) and 165 (71%) symptomatic (Groups B-E) (Fig 9). Sixty-nine (30%) was diagnosed due to macroscopic hematuria (Group B), 17 (7%) due to urinary tract symptoms (Group C), 19 (8%) due to symptoms caused be metastasis (Group D) and 60 (26%) due to paraneoplastic symptoms and signs (Group E).

The diameter of the RCCs in Group A was 4.9±2.6 cm (range 2-12 cm), and in Groups B-E when grouped together 8.9±3.2 cm (range 3-18 cm). Broken down into the individual groups the diameters was as follows: Group B 8.9±3.2 cm (range 4-17 cm); Group C 8.3±3.5 cm (range 4-17 cm); Group D 8.4±3.0 cm (range 3-13 cm); and Group E 9.1±3.1 cm (range 3-18 cm). The size difference between Group A and Groups B-E tumors was significant (p<0.001).
No RCC that were diagnosed because of macroscopic hematuria were <4 cm in size. Only 3/165 (2%) of the tumors in group B-E were <4 cm in size: one in Group C and two in group E. Twenty-six of sixty-seven (39%) RCCs in group A were <4 cm.

The incidental RCCs were less advanced, with lower TNM stages and a generally higher tumor differentiation. None of the incidental RCCs caused tumor thrombi. In Groups B-E, a tumor thrombus was found in 39 patients (24%) with tumor diameters measuring 9.7±2.8 cm (range 5-17 cm). Seven of the 232 patients (3%) had multiple RCCs (3 in Group A, 4 in groups B-E).

**Figure 9:**
Symptomatic RCCs tended to be 4 cm or larger.
Paper III

Image quality - unenhanced group

In the unenhanced group, 20 patients were included at the 20 mAs level without loss of clinically important information in any of the examined patients. No urinary tract calcifications were missed in the low dose UP images (UPL) compared to the normal dose UP images (UPN) (Fig 10). Fewer urinary tract anatomic structures could be delineated on UPL than on UPN images. However, all structures could be delineated when UPL images were viewed together with CMP images.

No urinary tract calcifications were missed in the UPL compared to the UPN. Using the CMP for anatomic reference helped to improve diagnostic confidence.

The mean diagnostic confidence was 3.7±0.9 (range 2-5) after viewing the UPL; 4.8±0.4 (range 4-5) after the UPN and 4.9±0.3 (range 4-5) after viewing the UPL in combination with the CMP. The diagnostic confidence was significantly lower for the UPL compared to the UPN (p<0.001). Combining the UPL and CMP resulted in significantly better diagnostic confidence than only considering the UPN image (p<0.05) (Fig 11).

The mean difference in attenuation in the liver, between the UPL and the UPN measurements, was 2.8±2.1 HU (range -1 to 7) and in the renal cysts 2.9±2.7 HU (range -3 to 8). Both in the liver and in cysts the mean attenuation value was higher in the UPL. Bland-Altman plots of the differences are seen in Fig 12.

Image quality – excretory phase group

The 20 reference eff. mAs level was abandoned after seven patients. Noisy images caused a reduced diagnostic confidence. Further, artifacts in the pelvis made it impossible to exclude small filling defects in the collecting system (Fig 13) in three patients. The diagnostic confidence was 3.1±0.9 (range 2 - 4) after viewing the low dose EP images (EPL), 4.3±0.7 (range 3 - 5) after the normal dose EP images (EPN) and 4.4±0.5 (range 4 - 5) after viewing the EPL+CMP. The diagnostic confidence was significantly lower for the EPL compared to the EPN (p<0.01). Combining the EPL and CMP was not significantly different from only considering the EPN image (p=0.53) (Fig 11).

Twenty patients were included at the 40 mAs level with no patient judged a failure. The diagnostic confidence after EPL was 4.0±0.7 (range 3 - 5), EPN 4.4±0.5 (range 4 - 5) and EPL+CMP 4.6±0.5 (range 4 - 5). The diagnostic confidence was significantly lower for the EPL compared to the EPN (p<0.001). Combining the EPL and CMP resulted in significantly better diagnostic confidence than only considering the EPN image (p<0.01).
The mean difference in attenuation in the liver, between the EPL and the EPN measurements, was 1.4±2.5 HU (range -4 to +6) and in the renal cysts 0.9±3.5 HU (range -5 to +9). Both in the liver and in cysts the mean attenuation value was higher in the UPL. Bland-Altman plots of the differences are seen in Fig 14.

The total effective dose from CTU could be reduced by 42%, from 16.2 mSv to 9.4 mSv, with a combination of normal dose corticomedullary phase with low-dose unenhanced and excretory phases (Table 4).

Figure 10:
A - low dose unenhanced scan (20 reference eff. mAs), B - normal dose unenhanced scan (100 reference eff. mAs), C - low dose unenhanced scan (20 reference eff. mAs), D - normal dose corticomedullary phase scan (120 reference eff. mAs).
Figure 11:
Distribution of diagnostic confidence in patients with low dose, normal dose and low dose in combination with corticomedullary phase.
(UP= unenhanced phase, EP= excretory phase, CMP= corticomedullary phase)

Figure 12: Unenhanced phase
The differences between attenuation measurements in the liver and renal cysts in low and normal dose images shown in Bland Altman plots.
Figure 13:
Increased image noise made it difficult to rule out small urothelial cell carcinomas in the collecting system on 20 eff. mAs level in the excretory phase. After 7 patients the 20 mAs level was abandoned. Image quality was satisfactory in the 40 eff. mAs level.
Table 4: CTDIvol and Effective Dose calculated with ImPACT CT Patient Dosimetry Calculator (version 1.0.2). CTDIvol values refer to actual delivered mean effective mAs and not to the reference effective mAs values set prospectively in CARE Dose. (UPN= unenhanced phase normal dose, UPL= unenhanced phase low dose, CMP= corticomedullary phase, EPL= excretory phase low dose, EPN= excretory phase normal dose)

<table>
<thead>
<tr>
<th>实际平均射线负荷 (eff. mAs)</th>
<th>CTDIvol (mGy)</th>
<th>有效剂量 (mSv)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UPL</td>
<td>17.6</td>
<td>1.5</td>
</tr>
<tr>
<td>UPN</td>
<td>84.8</td>
<td>7.0</td>
</tr>
<tr>
<td>CMP</td>
<td>114.0</td>
<td>9.4</td>
</tr>
<tr>
<td>EPL (40mAs)</td>
<td>33.2</td>
<td>2.7</td>
</tr>
<tr>
<td>EPN</td>
<td>83.6</td>
<td>6.9</td>
</tr>
</tbody>
</table>

Figure 14: Excretory phase

The differences between attenuation measurements in the liver and renal cysts in low and normal dose images shown in Bland Altman plots.
Paper IV

Changes in volume CT dose index (CTDI\text{vol}) and dose-length product (DLP) between 1997 and 2008 are presented in Table 5. The resulting changes in mean effective dose between 1997 and 2008 are presented in Table 6.

A reduced number of scans resulted in a reduction of the mean effective dose from 29.9/22.5 mSv (females [F]) / (males [M]) in 1997 (group A) to 26.1 / 18.9 mSv [F / M] (group B). The mAs settings were adapted to patient size in 2001 resulting in a reduction of CTDI\text{vol} from 11.1 to 7.1 and a reduction of the mean effective dose to 16.8 / 12.0 mSv [F / M] (group C). In 2005 (group D) the mean effective dose increased, to 18.2 / 13.1 mSv [F / M]. In 2008 (group E), the mean effective dose was reduced to 11.7 / 8.8 mSv [F / M].

Table 5: Values of CTDI\text{vol} and DLP for patients in groups A - E

<table>
<thead>
<tr>
<th>Group</th>
<th>Native phase</th>
<th>Corticomедullary phase</th>
<th>Nephrographic phase</th>
<th>Excretory phase</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CTDI\text{vol}</td>
<td>DLP mGy • cm</td>
<td>CTDI\text{vol}</td>
<td>DLP mGy • cm</td>
<td>CTDI\text{vol}</td>
</tr>
<tr>
<td>A</td>
<td>11.1</td>
<td>443</td>
<td>11.1</td>
<td>221</td>
<td>11.1</td>
</tr>
<tr>
<td>B</td>
<td>11.1</td>
<td>443</td>
<td>11.1</td>
<td>443</td>
<td>n.a.</td>
</tr>
<tr>
<td>C</td>
<td>7.1</td>
<td>285</td>
<td>7.1</td>
<td>285</td>
<td>n.a.</td>
</tr>
<tr>
<td>D</td>
<td>6.9/7.1*</td>
<td>278/285*</td>
<td>9.4/9.5*</td>
<td>376/381*</td>
<td>n.a.</td>
</tr>
<tr>
<td>E</td>
<td>3.6/3.4*</td>
<td>142/137*</td>
<td>7.2/6.9*</td>
<td>290/278*</td>
<td>n.a.</td>
</tr>
</tbody>
</table>

*Male/female.

n.a.: not applicable.

Table 6: Mean effective doses to patients in groups A - E

<table>
<thead>
<tr>
<th>Group</th>
<th>Native phase</th>
<th>Corticomедullary phase</th>
<th>Nephrographic phase</th>
<th>Excretory phase</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>6.3/8.7</td>
<td>6.3/8.7</td>
<td>n.a.</td>
<td>6.3/8.7</td>
<td>18.9/26.1</td>
</tr>
<tr>
<td>C</td>
<td>4.0/5.6</td>
<td>4.0/5.6</td>
<td>n.a.</td>
<td>4.0/5.6</td>
<td>12.0/16.8</td>
</tr>
<tr>
<td>D</td>
<td>3.9/5.5</td>
<td>5.3/7.4</td>
<td>n.a.</td>
<td>3.9/5.3</td>
<td>13.1/18.2</td>
</tr>
<tr>
<td>E</td>
<td>2.0/2.7</td>
<td>4.1/5.4</td>
<td>n.a.</td>
<td>2.7/3.6</td>
<td>8.8/11.7</td>
</tr>
</tbody>
</table>

*Male/female.

n.a.: not applicable.

Calculations were performed with identical scandata for males and females in groups A - C. In groups D and E, the mean mAs for males and females were used to calculate the effective dose.

n.a.: not applicable.
Discussion

By the end of the 1990s, it was apparent that the IVP would be replaced by CTU as the method of choice investigating patients with a suspected malignancy in the urinary tract. Because of the increased radiation dose from CTU, measures were needed to reduce the radiation dose. The focus of this thesis is on reducing the radiation dose from CTU. Papers I and III are directly aimed at reducing the radiation dose. Paper II was aimed to investigate what size renal cell carcinomas are when they cause symptoms an indirectly to see if the decision to discontinue the nephrographic phase was unwise. When paper IV was produced there was a lot of focus on the increased use of multidetector row CT and the high radiation dose. The results from paper IV shows that although the total number of CT examinations are increasing - the effective radiation dose to individual patients undergoing CTU in 2008 is only 39% of the radiation dose in 1997.

The impact of the papers on the CTU protocol

From four to three

The results from paper I suggest that the NP scan provide the least unique information. Following study I the first step was taken to reduce the radiation dose to patients undergoing CTU. The decision to discontinue the NP was controversial in the uroradiology world as most centers instead abolished the CMP scan. The choice was made although it had been shown that the NP scan detected an increased number of small (<3cm) medullar renal tumors compared to the CMP scan (39). The rationale behind our decision was based partly on the results of paper I, and on the experience that the CMP scan has several advantages over the NP scan. There is more dynamic information to be had from the CMP when evaluating renal stasis, and also vessel anatomy is more easily evaluated. A majority of RCCs are hypervascular (40) and therefore easily detected in the CMP. As all patients with renal and urothelial malignancies, as part of preoperative work-up, undergo CTU we realized that UCC enhance early following i.v. contrast injection and can be detected in the CMP scan.

Technical development has been rapid since the mid 90s. A recent literature search could not find any new multidetector row CT reports investigating the ability to detect small (<3cm) renal in the CMP and NP scans. Johnson et al (41) repeat in a short review in 2010 that the NP is superior for RCC conspicuity and detection, citing the same studies published in the 90s. One must however remember that although the diagnostic confidence for small renal tumors is highest in the NP scan, a study by...
Kopka at the time concluded that the best yield in RCC detection, characterization and staging is not reached by NP scan alone but with a combination of UP, CMP and NP scans (42).

Surgical techniques have also evolved; an increased number of RCCs are treated with partial nephrectomy or laparoscopic nephrectomy. The CMP is important for urologists planning partial nephrectomy as it provides a vascular map. Percutaneous treatment with cryoablation or RF-ablation is also increasing and operators also benefit from information from the CMP. In our experience, use of split bolus (i.e. contrast injected as two separate portions, creating a combined nephrographic and excretory phase) protocols reduces the diagnostic confidence in small renal and inter-determinate masses and UCC detection. The diagnostic confidence is reduced as less unique imaging information is available in a 2-phase examination and the excreted contrast can cause beam hardening artifacts making subtle mucosal lesions difficult to evaluate. A literature search found no studies comparing standard multiphase CTU protocols with split bolus techniques in mass detection or diagnostic confidence.

Finally, the UP-CMP-EP protocol has now been in use 10 years at Uppsala University Hospital. As there are no alternative hospitals in our area, missed tumors would be referred back again and give us feedback that the UP-CMP-EP protocol is suboptimal.

There are no international, or even Swedish, consensuses on how to perform a CTU. There are many “controversial” issues; the compromise between image quality and radiation exposure, justifications/indications, split-bolus injection, compression, saline infusion, low-dose diuretic administration, hybrid scanning, timing of the acquisition delay, examination protocols, postprocessing (43), and application of dual energy imaging (44, 45), with time the number of issues on which experts disagree only seem to increase.

There are two major standpoints on how to design a CTU protocol. One can, as in Uppsala, use the multiphase CTU as a “one-stop-shop” with excellent diagnostic capabilities in all patients. Or instead mold the CTU into an IVP performed with CT by performing split bolus CT, focusing on the excretory phase scan.

Kekelidze et al (46) recently presented an article where they in the introduction used a few common arguments to use the CTU as an CT-IVP; “A recently developed CT urographic technique can image the entire urinary tract in one acquisition, providing intravenous urogram-like images in a coronal reformatted view” and on the drawbacks of multiphase CTU “In addition, increased numbers of images are acquired and must be reviewed by radiologists”. The IVP was a straightforward examination that the radiologist did not have to tailor in advance to the individual patient, and the
examination then took the radiologist only a few minutes to review, often faster. And there were a maximum of 14 standard images for the radiologist to review. Yes, the IVP was a quick examination for the radiologists. That was not true for patients and nurses. Patients had to spend time prior to the examination to clean the bowels and in the examination room the usual examination time was 30–45 minutes compared to approximately 15-20 minutes for multidetector row CTU.

In a multiphase CTU with reformats in axial, coronal and sagittal planes and sometimes also thin slices to review the number of images that the radiologist must review are 2000 or more. And as there are radiation dose considerations with CTU, each examination must be tailored according to the question from the referring clinician and also according to the age and history of the patient and the number of previous CT examinations must be considered especially in younger patients. This process can be time consuming.

In other words the CT-IVP supporters choose to look past the possibilities of CT and seek to create a compromise between the swiftness of the IVP and diagnostic capabilities of CT. A CT-IVP produces fewer images for the radiologist to review and enabling the radiologists to work faster.

**Conclusion Paper I**

The cortical CT phase is best for characterizing renal parenchymal tumors and for determining normal variants of renal anatomy and the renal veins are best visualized in the cortical phase. The caval vein is impossible to evaluate in the cortical phase due to contrast medium flow artifacts. The effectiveness of the nephrographic and the excretory phases is equal in terms of detecting and characterizing renal lesions. One of these phases is needed not to miss small lesions located centrally in the kidney and to detect a tumor thrombus in the caval vein. The excretory phase provides more information on renal function than the nephrographic phase.

The number of solid lesions in the material is too small to permit any definite conclusions. However, it seems as if the nephrographic phase is the phase with the least unique diagnostic information.

**Is the sensitivity of CTU needed when examining patients with suspected RCC?**

Were we missing small RCCs with the UP-CMP-EP protocol? Paper II was performed as an attempt to evaluate this. Symptoms and signs suggestive of a urinary tract malignancy cause patients to seek medical help and be referred for CTU. If the patients have no clinical symptoms or signs suggestive of a urinary tract malignancy they will not seek medical help and they will not be referred for CTU.
The most common malignancy in the urinary tract in patients presenting with hematuria is carcinoma of the bladder, followed by RCC and upper urinary tract UCC (47) (Sjöblom et al, The Diagnostic Panorama in Patients with Gross Hematuria Examined with CT, poster ESUR 2006, Cairo) and the most common upper urinary tract malignancy is RCC. When discussing the CTU protocol, the following question is fundamental - “how large must a RCC be to cause hematuria or other symptoms suggestive of RCC?” A literature search found that there are reports, which present small symptomatic RCCs (48-50). A retrospective study was decided to evaluate the decision to discontinue the NP scan in favor of the CMP scan. Of course, no definite answer to the question was to be expected.

The results from Paper II show that RCCs tend to be 4 cm or larger before causing symptoms. None of the patients with hematuria diagnosed with RCC between 1996 and 2003 had a RCC smaller than 4 cm. The results gave us confidence in our decision to discontinue the NP scan. In other words, most small RCCs (<4cm) tend to be incidental tumors that are detected only with screening or as unexpected findings when patients undergo work up because of other complaints, as the tumor itself do not cause symptoms and signs suggestive of urinary tract malignancy. This said with knowledge of the limitations in this retrospective study, and the important issue of multifocal RCC (51, 52) which is reported to be present in up to 25% of cases (53).

**Conclusion Paper II**

Our results suggest that small (<4 cm) RCCs are asymptomatic. Therefore, if a 2-cm RCC is found in a patient complaining of macroscopic hematuria it is unlikely that this small RCC caused the hematuria. Another cause, such as urothelial cell carcinoma of the bladder (a more common malignancy than RCC), must be ruled out. It should be mentioned that the results of this retrospective study differ somewhat from those of other studies. These inconsistencies in findings underscore the need for additional future prospective studies examining whether small RCCs do or do not cause macroscopic hematuria or other signs suggestive of urinary tract malignancy.

**How low can we go?**

In the early 2000s attention was turned to the radiation dose from CT (25, 26). Soon individualized mAs settings, according to patient size, became clinical routine (54). In 2003 Tack et al published, “Low-dose unenhanced multidetector CT of patients with suspected renal colic” (55). Unenhanced CT performed with a very low radiation dose could be used to evaluate patients with suspected calculi. Unenhanced CT
with ultra low-dose settings caused far less radiation then the IVP, 1.2 mSv when performed with an tube load of 30 mAs compared to 2.5 – 3.5 mSv from an IVP, and requires no patient preparations. Reduced tube load ought to be possible also in the EP. Kemper et al (56) showed that the tube load in EP could be reduced to 70 eff. mAs.

It was not until 2005 when there was a general consensus that CTU is as good as the IVP to detect UCC in the renal collecting system and the ureters (14, 15). Many different techniques are suggested to optimize UCC detection in the upper urinary tract during the excretory phase in order to achieve optimal opacification and distension. These techniques include abdominal compression (15), a combination of prone and supine positioning, patient movement, i.v. saline infusion (14), oral administration of water, IV furosemide injection, and longer delay of imaging acquisition (15). One could argue that it would be unwise to reduce the tube load settings in the EP as there still was some uncertainty of the abilities of CTU to detect UCC in the upper urinary tract.

The Uppsala CTU protocol includes UP, CMP and EP scans and the patients are hydrated and given low dose i.v. furosemide. Small UCCs in the distended bladder and the upper urinary tract can be detected also in the CMP (M. Helenius, personal communication). As UCC in the EP is detected as filling defects in the contrast excretory system, it is similar to the situation in the UP where a high attenuation calculus is easily detected against the surrounding low attenuation soft tissues. I.e. there is high contrast differentiation between the high attenuation opacified urine and the low attenuation UCC.

The novel concept behind paper III was to mix low- and normal dose scans in the multiphase CTU. The most important scan for tumor detection and surgical planning is the CMP, and Tack (55) and Kemper (56) have already shown that reduced mAs settings is possible in the UP and EP scans. The dose-escalation study design was chosen in order to reduce the number of patients that needed to undergo additional low dose scans in the UP and EP.

The results were encouraging as the novel concept of a combined low and normal dose three phase CTU promise to reduce the radiation dose to the individual patient by 42%. The results has not been fully incorporated into clinical practice, the quality reference mAs settings are today reduced in the UP and EP scans compared to the CMP scan (paper IV). The strategy to reduce the image quality in all but one phase in a multiphase CT examination could probably in some degree also be adapted in CT imaging protocols of other parts of the human body (for example in multiphase brain-, liver-, adrenal-, and pancreas examinations).
Conclusion Paper III

In conclusion, it is possible to reduce the total CTU radiation dose by 42% when selectively reducing the dose in the UP and EP when the images from these phases are systematically evaluated alongside those of a normal dose CMP.

What really happened the last 10 years?

In Paper IV we look back at the past 10 years. What really happened between 1997 and 2008? Only ten years ago the term CT Urography did not exist. This study was decided in an attempt to structure the events of the last 10 years and decide which of the changes in CT technology and protocol that influenced the effective dose.

Early in 2008, a new CT scanner replaced the last remaining IVP laboratory at Akademiska Sjukhuset. This means that EU examinations are no longer performed routinely, and that all patients previously examined with IVP now undergo CT. The study clearly shows that although there is an increased use of CTU as it has replaced the IVP completely, the mean effective dose to the individual patients undergoing CTU is sixty percent lower in 2008 as compared to 1997. The reasons for this reduction of the mean effective radiation dose are not clear-cut, but it is obvious that reduced mAs settings have been key. It seems strange today that individualized scanning protocols were not adapted earlier.

Conclusion Paper IV

In conclusion, modern CT imaging partly suffers from a bad reputation created by previous CT imaging. Overall, the results from this study show that the mean effective dose to individual patients undergoing CTU has decreased by 60% between 1997 and 2008. In relation to the increased collective radiation dose from CT it is important to stress this fact – the individual patient who undergo CT receives less radiation then 10 years ago. The findings should be communicated to radiologists, clinicians, and patients.
How to perform a CTU

CTU - lack of definition

CTU has due to the technical improvements previously described replaced IVP as the method of choice investigating patients with suspected urinary tract pathology. How should a CTU be performed? It is important to tailor the CTU protocol according to the age, risk factors and previous CT history of the individual patient.

In opposite, the IVP was used to answer all questions such as; is there normal anatomy, are there urinary tract stones, is there urinary stasis, is there a urinary tract malignancy? All these questions were answered with the same, approximately, 10 (without compression) to 13 (with compression) standard images.

Radiation dose

Due to the relatively high radiation dose, the CTU must in contrast to the IVP, be tailored according to the age of the patient and the question from the referring clinician. A young individual <40 years old who undergo uroradiological workup have a low probability of a urinary tract malignancy and the focus must be to establish normal anatomy, presence of stones and normal excretion of contrast. Older patients, especially with alarming symptoms such as hematuria, have a high probability of urinary tract malignancy and the CTU protocol must be tailored to rule out a malignancy. These patients referred for imaging because of suspected urinary tract malignancy are often aged and therefore less sensitive to radiation. A recent study on patients investigated because of macroscopic hematuria at our department by Sjöblom et al, showed that the mean age is 66±14.5 (range 19 – 97) years (“The Diagnostic panorama in patients with gross hematuria examined with CT”. Poster presentation ESUR 2006, Cairo, Egypt).

Patients with suspected or known urinary tract stones are of special concern as these patients are often young and many patients return again and again and require repeated CT examinations. The radiologist, who decides the CTU protocol, must in each patient investigate if the patient has had previous CT examinations. And then, in order to avoid unnecessary radiation, take this knowledge into consideration as well as the ALARA dogma when deciding the CTU protocol.

In addition there are two more groups of patients who undergo CTU; patients undergoing follow up after surgery for RCC and treatment of UCC. Non-ionizing methods such as MR or US must always be considered to young individuals and patients undergoing repeated examinations.
Experts disagree on the CTU protocols to all of these groups. The Dutch society of urology suggests an algorithm that might be helpful, dividing patients by age and according to the likelihood of malignancy (57). The CTU can if tailored according to the needs and clinical background of each patient, serve to investigate all of these groups of patients without causing an unethically high radiation burden to the patients.

This thesis focuses on patients undergoing workup for suspected malignancy. How should the CTU be performed in this group? Radiation issues must be considered also in this group. Interestingly Paper II implies that in the case of symptomatic RCCs CTU probably is too sensitive. If a patient present with symptoms of RCC tumors are large enough to be detected also on IVP and US. One could argue that CTU would be most useful to detect non-symptomatic RCCs that are <4cm, however CTU has advantages to IVP and detecting calculi and to US detecting UCC.

**Tumor detection**

The Uppsala CTU protocol consists of three scans performed in the unenhanced, corticomedullary and excretory phases. The protocol differs from most other suggested three phase protocols, which include a nephrographic phase scan instead of the corticomedullary scan. It also differs from the split-bolus protocols, which rely on the unenhanced scan and a combined nephrographic/excretory phase scan (58). The most important reason to perform a nephrographic phase scan is that an increased number of small renal tumors are detected (39).

Even if this might not be important in symptomatic patients where RCCs tend to be 4 cm or larger (Paper II) (59) there is the issue of multifocal RCCs. In our material, which was collected partly before the change from 4-phase CTU to 3-phase, 3% of RCCs were multifocal. The literature describe that 4-25% of RCCs are multifocal (51-53). Schlichter (60) compared CT detection of RCC to the number of RCCs in resected kidneys. CT found multifocal tumors in only 11 of 48 patients with multiple RCCs in the nephrectomy specimens. The average diameter of the missed tumors was 7 mm. CT technology has improved since then and hopefully CTU now perform better.

There is a need for further studies of the different scan phases of CTU to verify the now dated studies that show the nephrographic phase to be superior to corticomedullary phase in detecting small parenchymal tumors. A possible solution to be used in high-risk patients is to add a short scan of the kidneys in the nephrographic phase. The triple bolus protocols suggested which combine corticomedullary, nephrographic and excretory phase scans might be of value (46).
The standard three-phase CTU is used also in patients undergoing follow up after previous RCC or UCC treatment. RCC tend to recur with a similar contrast enhancement as the original tumor, i.e. a highly vascular RCC will most often be highly vascular when it recurs. The imaging characteristics of the original tumor ought to be taken into consideration when designing the CTU protocol.

**Optimal filling of the collecting system, including ureters (and bladder)**

In IVP times patients were subjected to “abdominal compression” were an external frame compressed the ureters onto the sacrum. The compression was necessary to achieve optimal filling of the upper urinary tract collecting system. Nowadays, ambitious radiologists try to rule out UCC not only in the upper urinary tract but also in the bladder (61).

McTavish et al (14) concluded that CTU with abdominal compression was superior to CTU without compression. More recent reports (15, 58) suggest that compression is not needed but a low dose of intravenous furosemide (10 mg) improves distension and opacification of the intrarenal collecting system. Intravenous hydration prior to CTU has been advocated by some authors (14, 15) however the ESUR guidelines (58) suggests not to use i.v. hydration. In Uppsala patients receive oral hydration (800 ml during 120 minutes prior to the examination and patients are told not to void. Then patients receive 10 mg furosemide at the start of the examination.

At ESUR 2010 it was suggested that in the definition of CTU should say that it must include an excretory phase performed with at least a 10 min delay. Curic et al (62) describe that an excretory scan 1 h after ingestion of 1000 ml water and approximately 12 min EP-delay achieve optimal filling of the collecting system including a filled bladder. A filled bladder potentially, especially in prone position, cause obstruction and improves opacification of especially the ureters (Dahlman et al; CT Urography in Prone vs Supine position - effects on contrast layering in the excretory phase scan; ESUR 2010, Belgium). This means that the contrast opacification of the bladder might be compromised if no auxiliary manoeuvres, such as turning the patient or having the patient walk around the CT scanner prior to the excretory scan.

**Conclusion – how to perform a CTU**

Younger patients with low probability of malignancy: Low dose unenhanced scan and split bolus combined arterial / excretory phase scan.

Stone patients: Low dose unenhanced scan. After looking into patient information and preferably also following questioning the patient what has happened lately? Is she still in pain / stone passage / current creatinine value etc. In selected cases, a small dose (for example 10 ml, 350 mgI/ml) of i.v. contrast and a short excretory phase spiral focused over the mid poles of the kidney to see if contrast is excreted or not.
Patients with suspected malignancy: Triphase CTU, low dose unenhanced, normal dose corticomedullary and reduced dose excretory phase scan from the diaphragm to the pubic symphysis.

It is important that a radiologist or the nurse/technician read the referral and look through the examination before the patient leaves the CT table. A repeat excretory phase scan might be needed, sometimes in prone position.

The patient preparation is an important issue. My suggestion is that the patients drink approximately 800-1000 ml of water in 1 hour prior to the exam and then empty the bladder 45 minutes before the exam. Unenhanced and corticomedullary phase scans are then performed in supine position where after the patients turns to prone position and then turns back to supine position just before the excretory scan, performed after approximately 15 minutes.
Conclusions

Overall
This dissertation has shown that the mean effective dose to individual patients undergoing CTU at Uppsala University Hospital has decreased by 60% between 1997 and 2008. This message is important to communicate in times when there is a lot of focus on the increased use of CT and the resulting increasing radiation dose to total population.

The individual studies in the thesis have contributed to this decrease in radiation dose.

Paper I
In four phase CTU, the effectiveness of the nephrographic and the excretory phases is equal in terms of detecting and characterizing renal cysts. The number of solid lesions in the material is small, however the cortical CT phase scored best for characterizing renal parenchymal tumors. The renal veins are also best visualized in the cortical phase. The nephrographic phase was judged as the phase that contributes with the least unique diagnostic information.

Paper II
Between 1996 and 2003 none of the RCCs diagnosed because of macroscopic hematuria was smaller than 4 cm. Hematuria is the most important reason why patients undergo multiphase CTU and these results gave confidence to continue the three phase CTU protocol including the unenhanced, corticomedullary and excretory phase.
Paper III
It is possible to perform three-phase CTU with a combination of low and normal dose scans. In multiphase CTU, all of the phases do not need to have excellent image quality.

The dose-escalation study showed that with the lowest possible tube load settings in the unenhanced and excretory phases the effective dose of 3-phase CTU could be lowered from 16.2 mSv to 9.4 mSv. This 42% dose reduction is possible if the low dose images are systematically reviewed alongside the normal dose corticomedullary phase images, which are used for anatomic reference.

The study also showed that attenuation measurements in low- and normal dose images are comparable and that attenuation measurements in low dose images can be used as baseline attenuation values when characterizing renal lesions in multiphase CTU.

Paper IV
In 1997 the effective radiation dose from a multiphase CTU was eight times higher than from an IVP. In 2008, the effective dose is only three times higher. The major contributor to the dose reduction is the introduction of individual scan protocols, adapting tube load settings to patient size.
**Comments on CTU**

It should be underscored that the patients who undergo multiphase CTU because of suspected malignancy are generally older patients and therefore less sensitive to radiation. A high percentage of the examined patients have an underlying malignancy.

Younger individuals and patients with suspected urinary calculi should not undergo the standard three phase CTU. Instead these patients ought to undergo tailored CTU protocols consisting of one or two phases. To these patients the effective dose from the CT examination is comparable to IVP.

**Future**

It is still not verified if low dose radiation cause cancer and there is an ongoing debate on the LNT-theory. Radiologist must act as if the LNT-theory is true and use ionizing radiation in diagnostic imaging with caution. As the use of CT increases, radiologists must be aware of the dose issue and avoid unnecessary radiation by using proper justification, especially to younger individuals. There is a need for integrated tools in the radiology information systems to keep track of the accumulated radiation dose in each patient. Such a tool would help radiologists to address this important issue.

The effective dose from CTU to individual patients examined at Uppsala University Hospital is low compared to other centers. The optimization effort will however continue. Also technical innovations promise to, when implemented into clinical practice reduce the radiation dose from CTU further.
Urografi har varit standardmetoden för att avbilda urinvägarna sedan 1930-talet. För tio år sedan började dock datortomografi av urinvägarna (CT urografi = CTU) att ersätta urografierna. På Akademiska sjukhuset i Uppsala utfördes sedan 2007 inte längre urografier rutinmässigt då det sista urografi-laboratoriet lades ned och ersattes av en CT scanner. CTU har många fördelar jämfört urografi då fler urinvägskonkrement liksom fler och mindre tumörer kan detekteras. CT diagnostiserar även traumatiska skador inom urinvägarna och njurbäckeninflammationer. Inför en urografiundersökning krävdes det av patienterna att de skulle rengöra tarmen (=laxera). Detta behöver ej patienterna göra inför CTU.

En datortomograf (=CT) är en röntgenapparat som snurrar runt patienten medan patienten passerar genom CT maskinens tunnel. En CTU undersökning består av upp till fyra svep (=kontrastmedelsfaser) genom patientens buk/bäcken. De fyra traditionella kontrastmedelsfaserna är: före kontrast (=nativ fas) (Fig 15, 1a+b) samt efter intravenös kontrastmedelsinjektion i kortikomedullär fas (efter 20-30 sek - när kontrasten hunnit passera till framförallt artärsidan i kärlträdet och till njurens kärl och njurbarken) (Fig 15, 2a+b), nefrografisk fas (efter cirka 70 sek - kontrasten har nu passerat till vensidan i kärlträdet och även tagits upp och finns i hela njuren) och utsöndringsfas (efter 5 min - kontrasten har nu utsöndrats i njurens urinuppsamlingsystem och passerat vidare ner till urinblåsan) (Fig 15, 3a+b).

Denna avhandling fokuserar på patienter med misstänkt cancer i urinvägarna. Ett av de vanligaste symtomen på urinvägscancer är makroskopisk hematuri. Dessa patienter undersöks med röntgen av de övre urinvägarna och urologerna utför en cystoskopi av urinblåsan.

CT har en stor nackdel jämfört med urografi då de undersökta patienterna blir utsatta för en betydligt högre stråldos. Syftet med avhandlingsarbetet var att sänka stråldosen från CT av urinvägarna. Resultaten från de olika delstudier som ingår i avhandlingen har bidragit till en avsevärd sänkning av stråldosen till de individer som genomgår en CTU. Den effektiva dosen är idag i genomsnitt cirka 10 mSv jämfört med 30 mSv 1997.

Arbete I

I studie I undersökte antal synbara cystor och tumörer i njurarna i de fyra olika kontrastmedelsfaserna. Varje fas granskades separat och resultatet visade att den nefrografiska fasen bidrog med minst unik information. Därefter avskaffades den nefrografiska fasen när antalet kontrastmedelsfaser vid CTU minskades från fyra till tre.
Arbete II

**Arbete III**

I studie III testades hur mycket man kan sänka stråldosen från en CTU om den utförs med en kombination av låg- och normal stråldos. Det borde gå att sänka stråldosen i både nativfasen och utsöndringsfasen om lågdosbilderna med sämre bildkvalité systematiskt bedöms tillsammans med bilder tagna med normal stråldos i kortikome-dullärfas. Resultatet visade att det med en kombination av låg- och normal stråldos var möjligt att sänka stråldosen vid 3-fas CTU med 42%, från 16.2 mSv till 9.4 mSv.

**Arbete IV**


**Sammanfattning**

Trots att stråldosen till hela befolkningen ökat då mer och mer CT undersökningar utförs har alltså stråldosen till de enskilda patienterna som genomgår CTU minskat med 60%. Vårt förbättringsarbete för att sänka stråldoserna så mycket som det är möjligt utan att förlora viktig information från bilderna fortsätter.

Vidare har det på senare tid presenterats flera tekniska lösningar vilka efter att de implementerats i vår kliniska vardag kommer att göra det möjligt att sänka stråldoserna ytterligare.

Ännu finns inget sätt att integrerat i de radiologiska datasystemen registrera varje patients ackumulerade stråldos. Det finns ett behov av ett sådant system vilket skulle hjälpa radiologerna att ta hänsyn till patienternas tidigare strålbelastning när en ny radiologisk undersökning planeras.
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*Subjects investigated: A comparison of CT and IVP in the detection of upper tract UCC. // An investigation, “Is the radiation dose increasing in uroradiology?”, aimed to calculate the total effective dose to all patients undergoing uroradiological work-up between 1992 and 2004. // A retrospective review of all kidney contrast enhanced ultrasound examinations to investigate why and how we use CEUS of the kidneys. // Creation of a bladder phantom, in order to study the layering effect between excreted iodinated contrast and urine. // Later a clinical follow up to the bladder phantom study where the layering effect in the bladder was compared in patients undergoing CTU in prone and supine position.
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