PROTEHCT

-PROspective Trial for Examining Hematuria using Computed Tompgraphy

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PROTEHCT
-main causes of interest

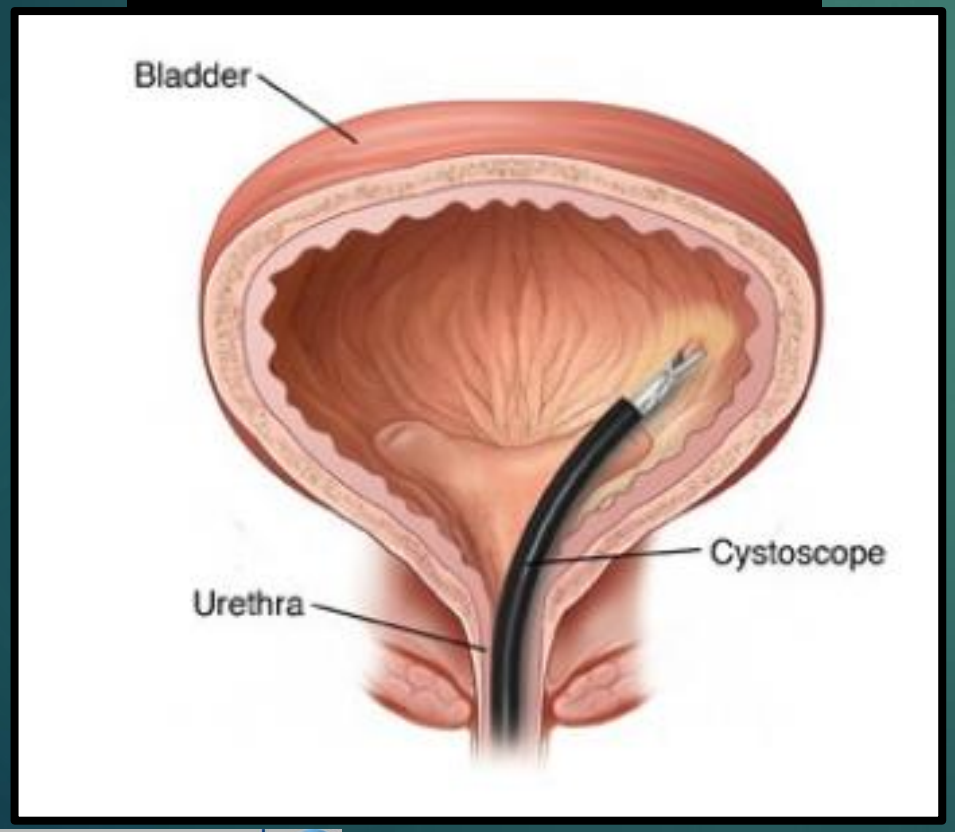
- Urothelial carcinoma (UC)
- Renal cell carcinoma (RCC)
- Urinary stone disease (USD)

BACKGROUND HEMATURIA

VISIBLE HEMATURIA (VH) WORKUP

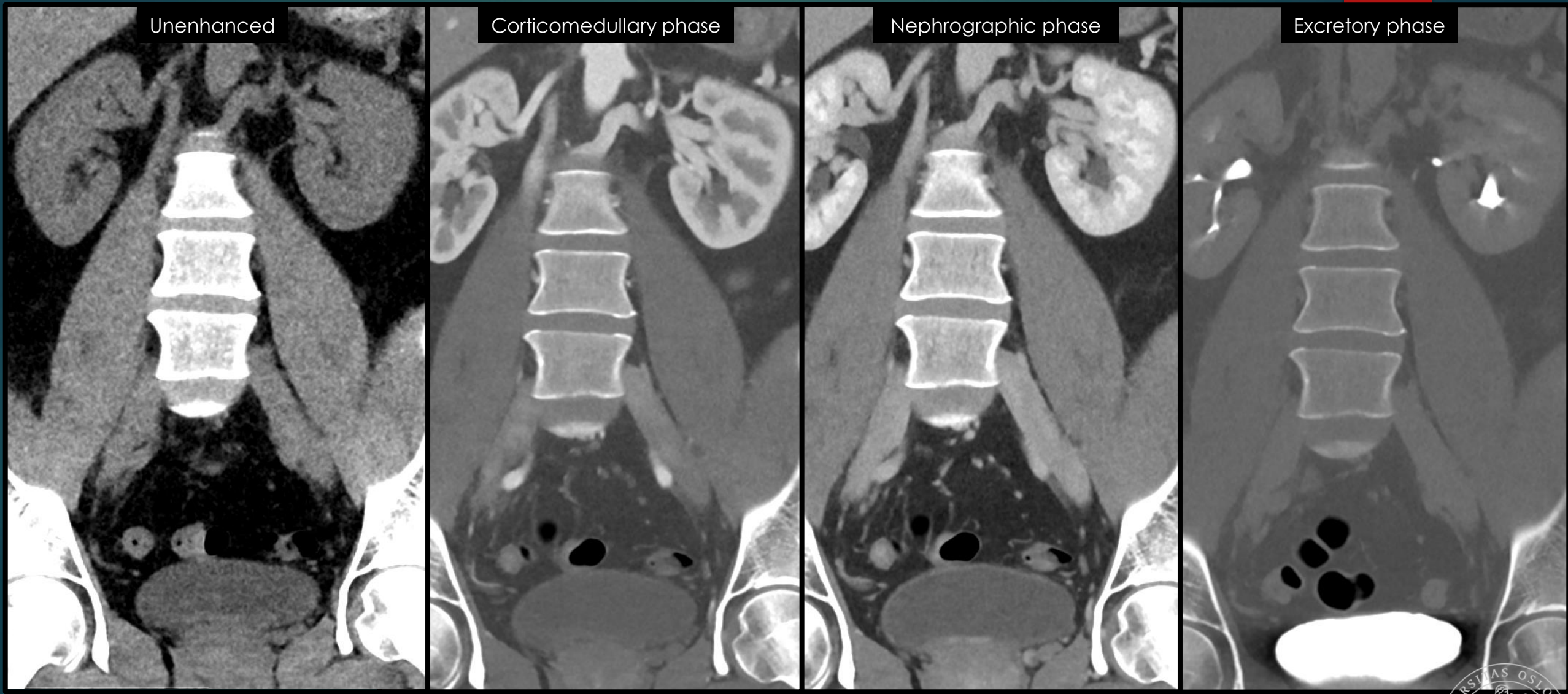
Bladder	Upper urinary tract
Urology	Radiology

Cystoscopy



Multiphase CT

BACKGROUND CT



BACKGROUND GUIDELINES

2008

2012

2016

2023

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Oncology guidelines

- Prostate Cancer
- Non-muscle-invasive Bladder Cancer
- Upper Urinary Tract Urothelial Cell Carcinoma
- Muscle-invasive and Metastatic Bladder Cancer
- Sexual and Reproductive Health
- Non-neurogenic Female LUTS
- Urethral Strictures
- Management of Non-neurogenic Male LUTS
- Chronic Pelvic Pain
- Urological Infections
- Neuro-urology
- Urolithiasis

Table 3 – Guidelines for UTUC diagnosis

Recommendation	Strength rating
Perform urethrocystoscopy to rule out bladder tumour.	Strong
Perform CT urography for diagnosis and staging.	Strong
Use diagnostic ureteroscopy (preferably without biopsy) if imaging and/or voided urine cytology are not sufficient for the diagnosis and/or risk stratification of patients suspected to have UTUC.	Strong
Magnetic resonance urography or ^{18}FDG-PET/CT (to assess [nodal] metastasis) may be used when CT is contraindicated.	Weak

CT = computed tomography; ^{18}FDG-PET = ^{18}F-fluorodeoxglucose positron emission tomography; UTUC = upper tract urothelial carcinoma.

Radiology

phase DECT were 1076±248 mGy·cm, 410±98 mGy·cm, DLP dose-length product

m, respectively (P<0.001).

, Toronto, ON, Canada; Department of Urol-

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Flerfase CT urinveier

Flerfase CT urinveier (CT urografi/ CT nyrer-urinveier-blære med kontrast/CT urinveier med kontrast- en undersøkelse med mange navn)

Dette er den primært valgte billeddiagnostiske undersøkelsen i utredningen av hematuri og nyre-/urinveiskreft, og anbefales brukt der det ikke er gode grunner for å la være, for eksempel svært redusert nyrefunksjon (med tanke på intravenøs kontrast), graviditet eller fare for alvorlig kontrastmiddelreaksjon (Heller & Tublin, 2014). Den brukes for å bekrefte om det foreligger kreft, for å stadieinndele kjent kreft, både lokalt og med tanke på metastaser, og for oppfølging av behandling/forløp (Maurer et al., 2013; Moloney, Murphy, Twomey, O'Connor, & Maher, 2014; O'Connor, Fitzgerald, & Maher, 2010).

a. Det er vanlig å ta serier gjennom det aktuelle området både uten og med intravenøs kontrast: Serien uten kontrast gjøres for å se etter konkrementer. Den er ikke obligat der man skal gjøre malignitetsutredning, da stein også vises på kontrastundersøkelsen. Den brukes også som utgangspunkt for å vurdere om en lesjon i nyrene lader kontrast eller ikke, dvs om den er perfundert, for å skille hyperdens cyste fra tumor og av og til annen ikke-neoplastisk prosess. Det varierer hvor stort område man undersøker (bare nyrene/komplett gjennom urinveiene), om det brukes lavdose, snitt-tykkelse med mer. Dersom man bare er ute etter urinveiene, kan denne serien sløyfes.
b. En eller flere serier med intravenøs kontrast i forskjellige faser etter hva man vil framstille, f.eks. arteriefase, der karanatomien er avgjørende, prosesser i nyreparenkymet som vurderes best i tidlig fase, som for eksempel infarkter, dessuten tyder flere studier på at blæretumores vurderes best i denne fasen (Helenius, Dahlman, Magnusson, Lönnemark, & Magnusson, 2014). Litt senere fase (nefrografisk-parenkym- portovenøs-mange navn) for å se etter svulster i nyrene, lymfeknuter, levermetastaser etc. Denne/disse fasene omfatter som regel både nyrer, urinveier og blære og det benyttes ordinær stråledose. Noen foretrekker positiv peroral kontrast for markering av tarm, andre ikke. Der man spesifikt skal vurdere nyreparenkym eller karanatomi, kan området begrenses. Blæren bør ikke være tom og ikke så full at det er smertefullt for pasienten.
c. Senfase/utskillelsesfase/ekskresjonsfase/urografifase: Serie som tas når ekskresjonen av kontrast har nådd ureteres/blære. Denne gjøres for å vurdere urinveisanatomi, evt obstruksjon og lesjoner i øvre urinveier og kontrastdefekter i blæren, selv om blæresvulster vises vel så godt på den tidlige fasen. Man kan variere stråledose, leie av pasienten, hvilket område som undersøkes, og på hvilket tidspunkt etter kontrast serien skal tas (oftest 5–10 minutter, men ved obstruksjon kan denne fasen komme inntil timer senere).
d. Noen kombinerer serie b og c ved å benytte «split bolus», dvs å gi deler av kontrasten først, deretter resten av kontrasten etter en gitt tid: 5–10 min, og deretter fotografere pasienten slik at man får begge faser i ett. Fordelen er redusert stråledose, ulempen er mindre kontrast pr. fase for å vurdere parenkym (nyrer/lever) og dårligere framstilling av samlesystemet pga. mindre kontrast i rett fase. Altså et slags kompromiss. Den kan brukes der det er helt avgjørende å redusere stråledosen.

Flerfase CT gjøres i mange varianter og serier, og ofte har man skreddersydd en flerfaseserie for den enkelte pasient avhengig av aktuelle problemstilling. Jo mer spesifikk problemstilling, jo bedre tilpasset undersøkelse (Takeuchi, Konrad, Kawashima, Boorjian, & Takahashi, 2015).

Der man benytter Dual energy-CT, kan man unngå serien uten kontrast, da man kan beregne en slik serie ut fra en kontrastundersøkelse. Vurderingen av om lesjoner har blodgjennom-strømning eller ikke, gjøres etter et annet prinsipp enn tetthetsmåling, og baserer seg på måling av jodforekomst (jodholdig kontrast).

lingene

spørsmål om kreft i øvre
arteriell) er sensitiv for
urinveier, er det imidlertid
s *Bruk av CT ved blærekreft*

A
C
tuelt

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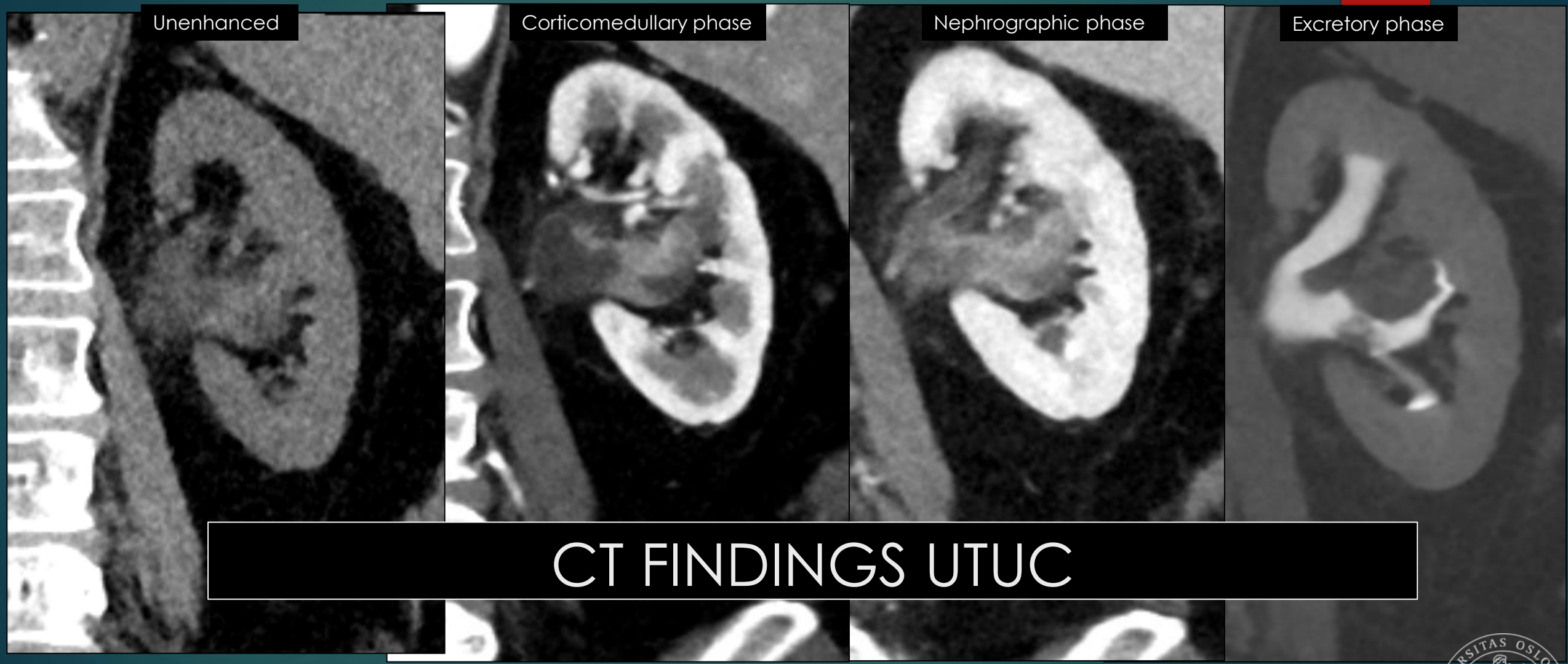

CT FINDINGS UTUC

BACKGROUND

2019

European Radiology (2020) 30:1664–1670
https://doi.org/10.1007/s00330-019-06521-0

COMPUTED TOMOGRAPHY

Examining the upper urinary tract in patients with hematuria—time to revise the CT urography protocol?

Erik Rud[1] · Kristina Flor Galtung[1] · Peter Mæhre Lauritzen[1] · Eduard Baco[2] · Tove Flatabø[1] · Gunnar Sandbæk[1]

In conclusion, CTU is highly accurate for the detection of upper urinary tract cancer, and all cases of both RCCs and UCCs were seen in the nephrographic phase. Our results suggest that the CTU protocol may be simplified, but prospective studies are needed. For this purpose, we are now starting the study Prospective Trial for Examining Hematuria with CT (PROTEHCT) (ClinicalTrials ID NCT04077359).

was 88% (95% CI, 47–99), and negative predictive value was 100% (95% CI, 99–100). The accuracy was 99% (95% CI, 96–100). All UCCs were visible on the nephrographic phase for both reviewers.

Conclusion CTU is highly accurate for detecting upper UCCs. All cases were seen on the nephrographic phase. This suggests that the CTU protocol can be simplified.

Key Points

- *CT urography is highly accurate for detecting upper urothelial cell carcinomas.*
- *All cancers were seen on the nephrographic phase.*
- *All cancers were detected in patients with macroscopic hematuria.*

Keywords Hematuria · Transitional cell carcinoma · Renal cell carcinoma · Urography

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BACKGROUND HEMATURIA

2022

EUROPEAN UROLOGY xxx (2022) xxx

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European Association of Urology

Review – Urothelial Cancer

Systematic Review of the Incidence of and Risk Factors for Urothelial Cancers and Renal Cell Carcinoma Among Patients with Haematuria

Bhavan P. Rai[a,*,†], *José Luis Dominguez Escrig*[b,†], *Luís Vale*[c], *Teele Kuusk*[d], *Otakar Capoun*[e], *Viktor Soukup*[e], *Harman M. Bruins*[f], *Yuhong Yuan*[g], *Philippe D. Violette*[h,i], *Nancy Santesso*[h,j], *Bas W.G. van Rhijn*[k], *A. Hugh Mostafid*[l], *Muhammad Imran Omar*[m]

VISIBLE HEMATURIA		
Bladder UC	UTUC	RCC
17% (95% CI: 14-20)	0.75% (95% CI: 0.4-1.2)	2% (95% CI: 1-2)

Article history:
Accepted March 17, 2022

Associate Editor:
James Catto

Keywords:
Haematuria
Urological neoplasms
Urinary bladder neoplasms
Kidney neoplasms
Smoking
Sex
Radiotherapy
Age distribution
Transitional cell carcinoma
Cystoscopy

Context: The current impact of haematuria investigations on health care organisations is significant. There is currently no consensus on how to investigate patients with haematuria.

Objective: To evaluate the incidence of bladder cancer, upper tract urothelial carcinoma (UTUC), and renal cell carcinoma (RCC) among patients undergoing investigation for haematuria and identify any risk factors for bladder cancer, UTUC, and RCC (BUR).

Evidence acquisition: Medline, Embase, and Cochrane controlled trials databases and ClinicalTrials.gov were searched for all relevant publications from January 1, 2000 to June 2021 according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. Prospective, retrospective, and cross-sectional studies with a minimum population of 50 patients with haematuria were considered for the review.

Evidence synthesis: A total of 44 studies were included. The total number of participants was 229 701. The pooled incidence rate for urothelial bladder cancer was 17% (95% confidence interval [CI] 14–20%) for visible haematuria (VH) and 3.3% (95% CI 2.45–4.3%) for nonvisible haematuria (NVH). The pooled incidence rate for RCC was 2% (95% CI 1–2%) for VH and 0.58% (95% CI 0.42–0.77%) for NVH. The pooled incidence rate for UTUC was 0.75% (95% CI 0.4–1.2%) for VH and 0.17% (95% CI 0.081–0.299%) for NVH. On sensitivity analysis, the proportions of males (risk ratio [RR] 1.14, 95% CI 1.10–1.17 for VH; 1.54, 95% CI 1.34–1.78 for NVH; $p < 0.00001$; moderate certainty evidence) and individuals with a smoking history (RR 1.41, 95% CI 1.24–1.61 for VH; 1.53, 95% CI 1.36–1.72 for NVH; $p < 0.00001$; moderate certainty evidence) appeared to be higher in BUR than in non-BUR groups.

† Joint first authors.
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E-mail address: urobhavan@gmail.com (B.P. Rai).

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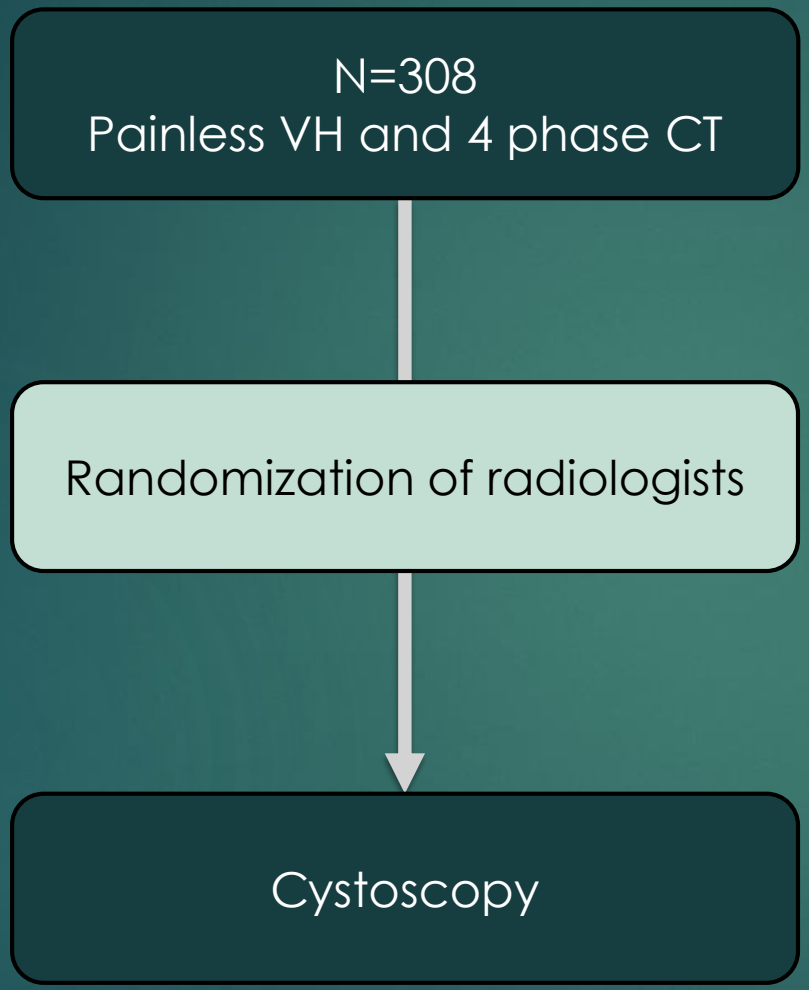
94-100% accuracy for detecting UTUC.
82-97% accuracy for detecting bladder UC.

Research question

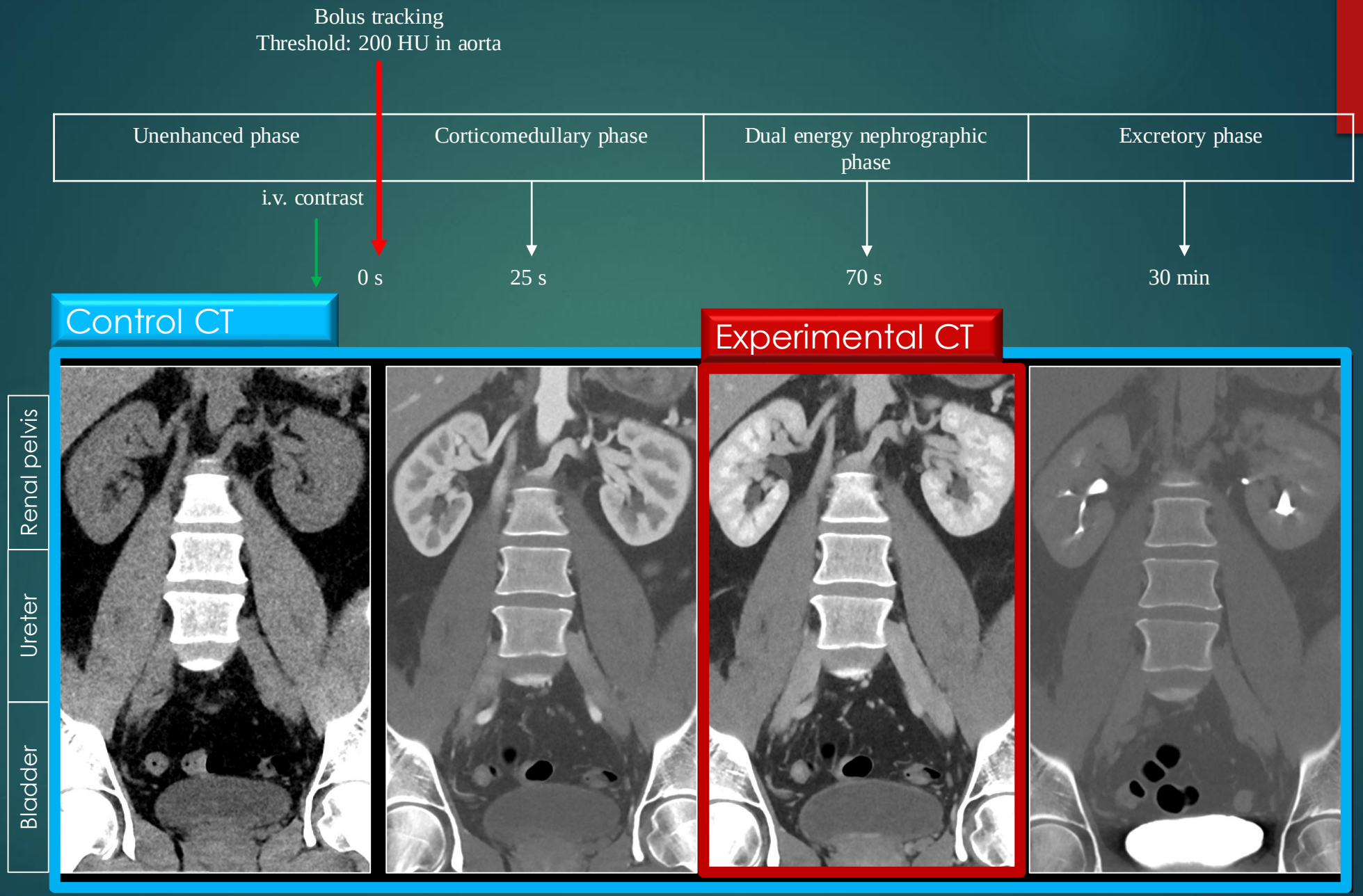
Is a single nephrographic phase CT sufficient for detecting urothelial carcinoma (UC) in patients with painless visible hematuria (VH)?

PROTEHCT Study Setup



- 81% men (250/308)
- Median age 68 y (IQR 53-77, range 18-96)

- 2 Reading Teams


Bolus tracking
Threshold: 200 HU in aorta
Unenhanced phase
Corticomedullary phase
Dual energy nephrographic phase
Excretory phase
i.v. contrast
0 s
25 s
70 s
30 min
Control CT
Experimental CT
Renal pelvis
Ureter
Bladder

CT Likert scoring

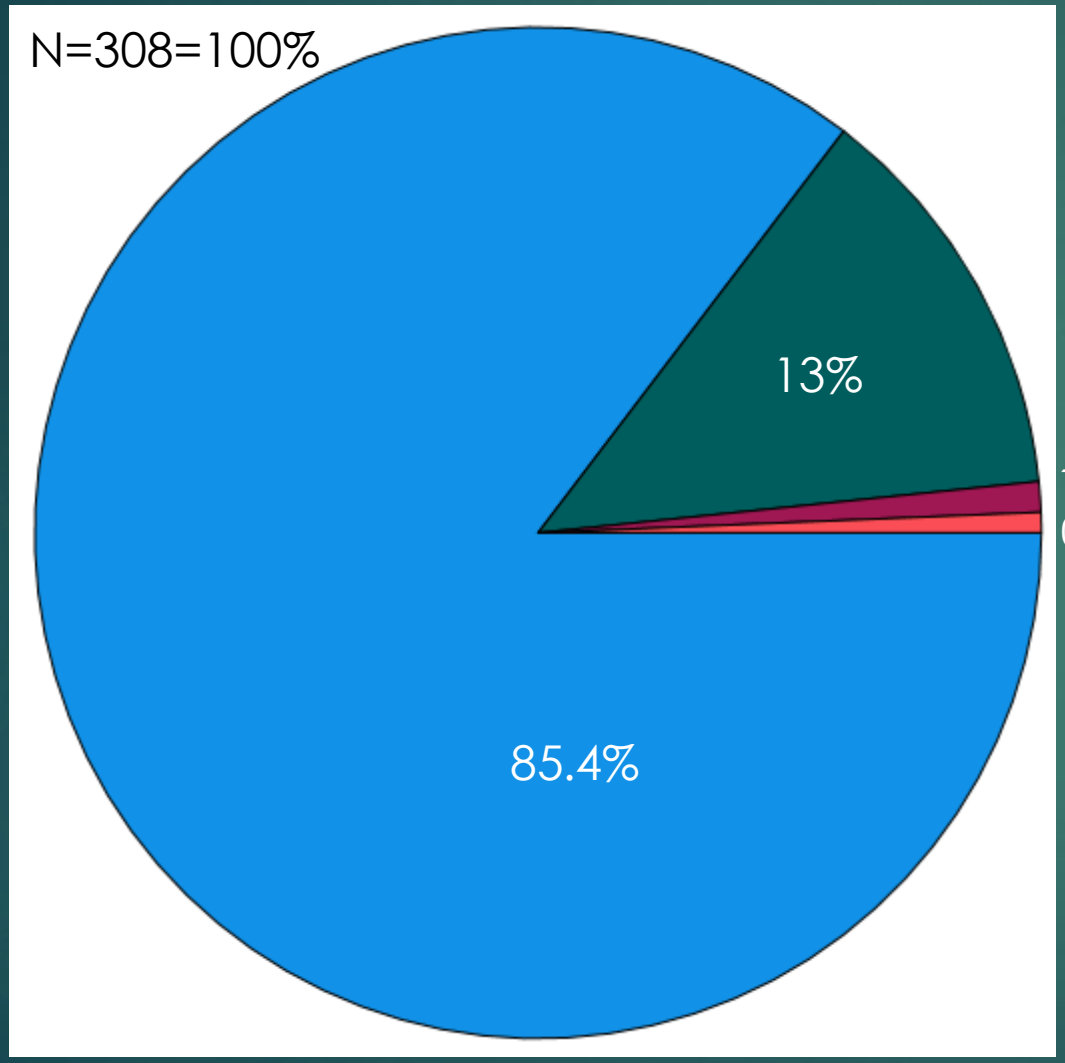
- 1= No UC
- 2= Probably no UC
- 3= Indifferent
- 4= Moderate suspicion of UC
- 5= Strong suspicion of UC

Negative CT

Positive CT

Reference standard: Final histology and 12 months follow-up.

RESULTS



No UC	(263/308)
Bladder UC	(40/308)
Ureter UC	(3/308)
Renal pelvis UC	(2/308)

No patients had synchronous UTUC and bladder UC.

RESULTS

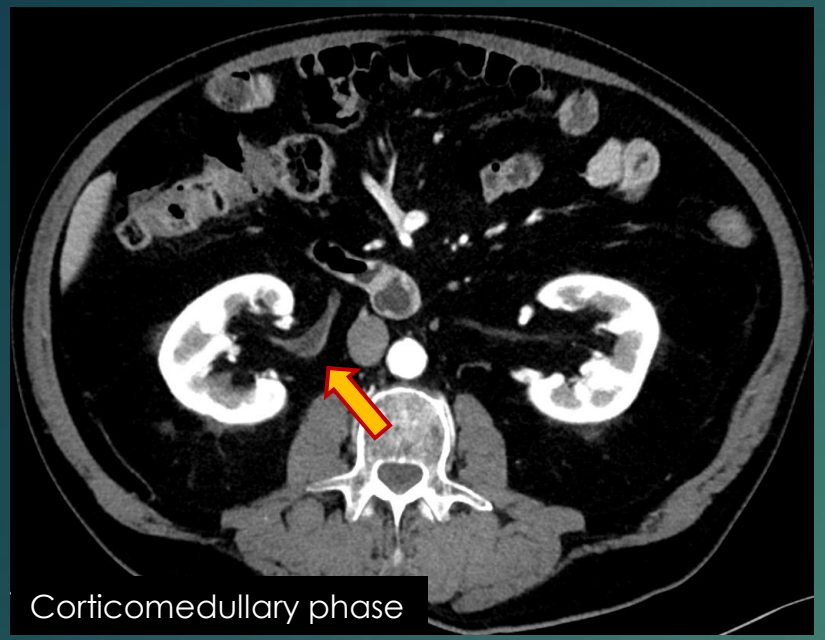
Bladder and Upper Urinary Tract

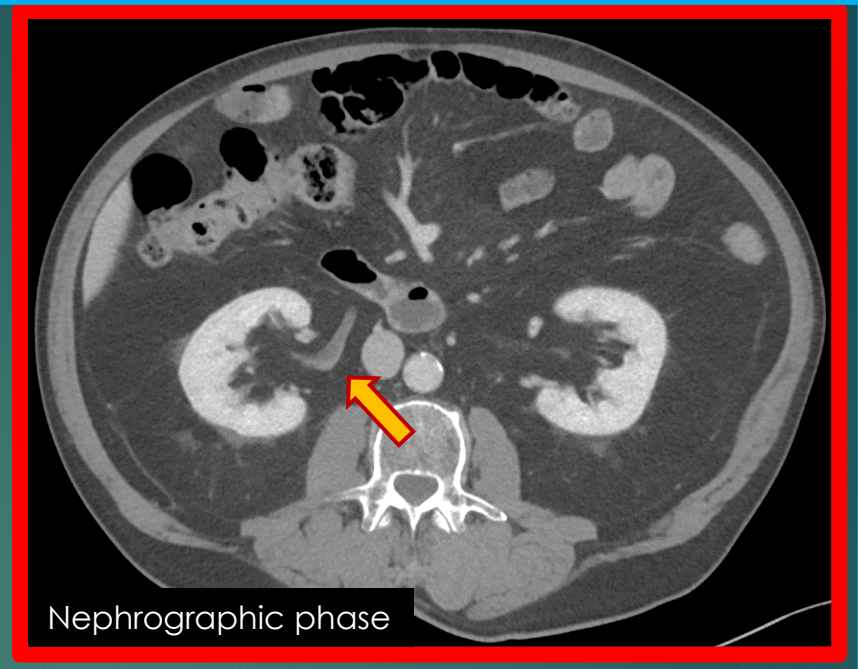
	Sensitivity (95% CI)	Specificity (95% CI)	NPV (95% CI)	PPV (95% CI)	Accuracy (95% CI)
Primary readers					
Control CT	93.3 (82-98)	83.7 (79-88)	98.7 (96-99.5)	49.4 (39-60)	85.0 (80.6-88.6)
Experimental CT	91.1 (79.3-96.5)	81.8 (76.6-86.0)	98.2 (95.4-99.3)	46.1 (36.1-56.4)	83.1 (78.5-86.9)
Difference	2.2 (-11.8 to 16.3)	1.9 (-4.9 to 8.6)	0.5 (-2.6 to 3.7)	3.3 (-12.1 to 18.5)	1.9 (-2.8 to 6.7)
Secondary readers					
Control CT	82.2 (68.7-90.7)	91.3 (87.2-94.1)	96.8 (93.8-98.4)	61.7 (49.0-72.9)	89.9 (86.1-92.8)
Experimental CT	82.2 (68.7-90.7)	92.8 (89.0-95.3)	96.8 (93.9-98.4)	66.1 (53.0-77.1)	91.2 (87.6-93.9)
Difference	0.0 (-17.5 to 17.5)	-1.5 (-6.6 to 3.5)	0.0 (-3.7 to 3.6)	-4.4 (-22.3 to 14.0)	-1.3 (-5.3 to 2.7)

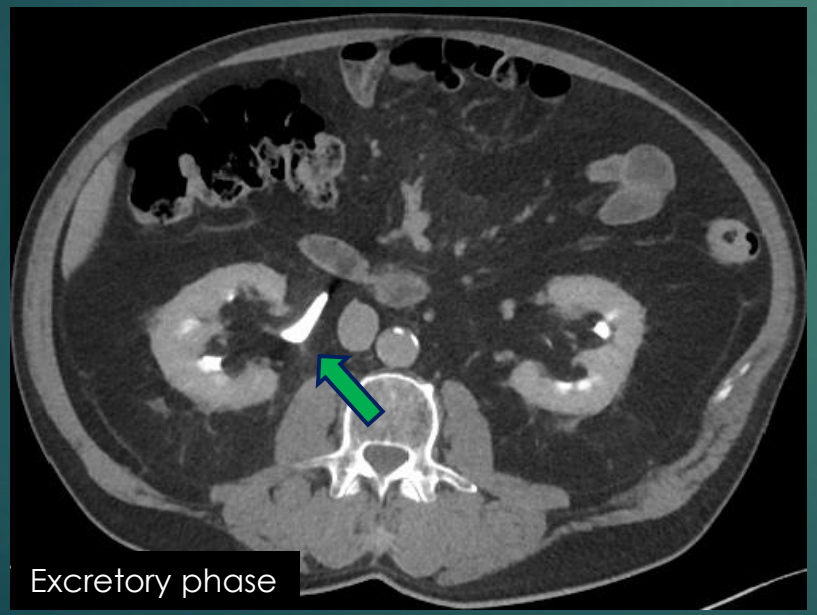
RESULTS

Upper Urinary Tract

	Sensitivity (95% CI)	Specificity (95% CI)	NPV (95% CI)	PPV (95% CI)	Accuracy (95% CI)
Primary readers					
Control CT	80.0 (37.6-96.4)	98.0 (95.8-99.1)	99.7 (98.1-99.9)	40.0 (16.8-68.7)	97.7 (95.4-89.9)
Experimental CT	80.0 (37.6-96.4)	97.0 (94.5-98.4)	99.7 (98.1-99.9)	30.8 (12.7-57.6)	96.7 (94.1-98.2)
Difference	0.0 (-53.6 to 53.6)	1.0 (-1.9 to 4.0)	0.0 (-1.8 to 1.9)	9.2 (-30.9 to 47.7)	1.0 (-1.6 to 3.7)
Secondary readers					
Control CT	80.0 (37.6-96.4)	97.7 (95.3-98.9)	99.7 (98.1-99.9)	36.4 (15.2-64.6)	97.4 (95.0-98.7)
Experimental CT	80.0 (37.6-96.4)	97.7 (95.3-98.9)	99.7 (98.1-99.9)	36.4 (15.2-64.6)	97.4 (95.0-98.7)
Difference	0.0 (-53.6 to 53.6)	0.0 (-2.9 to 2.9)	0.0 (-1.8 to 1.8)	0.0 (-40.0 to 40.0)	0.0 (-2.7 to 2.7)





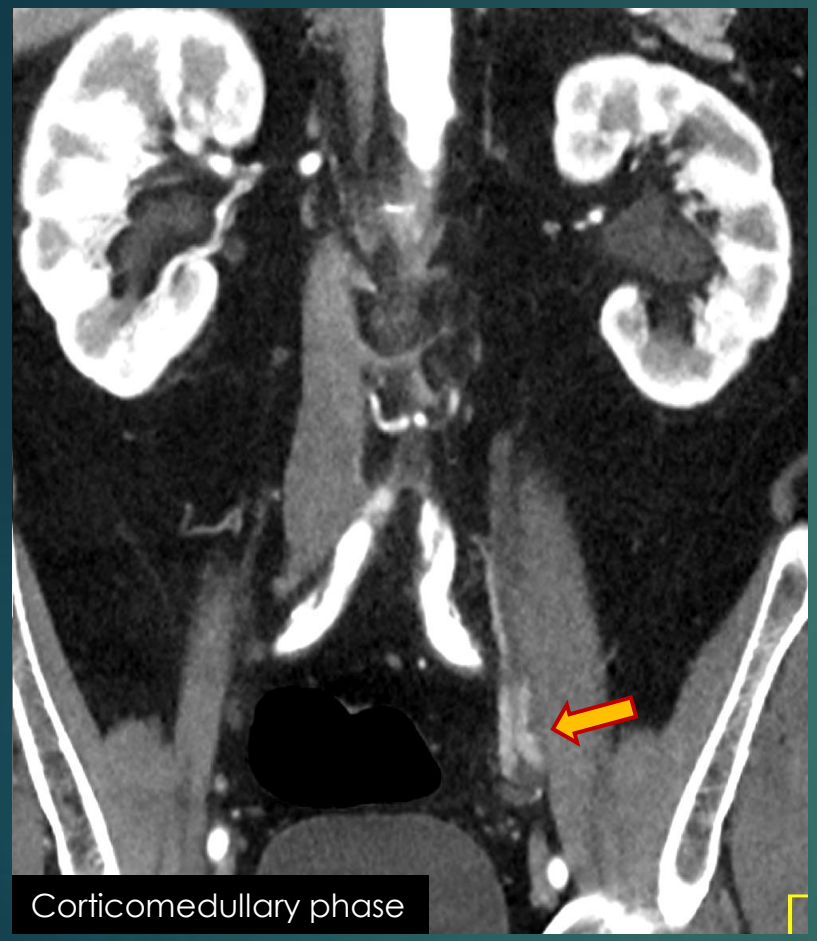


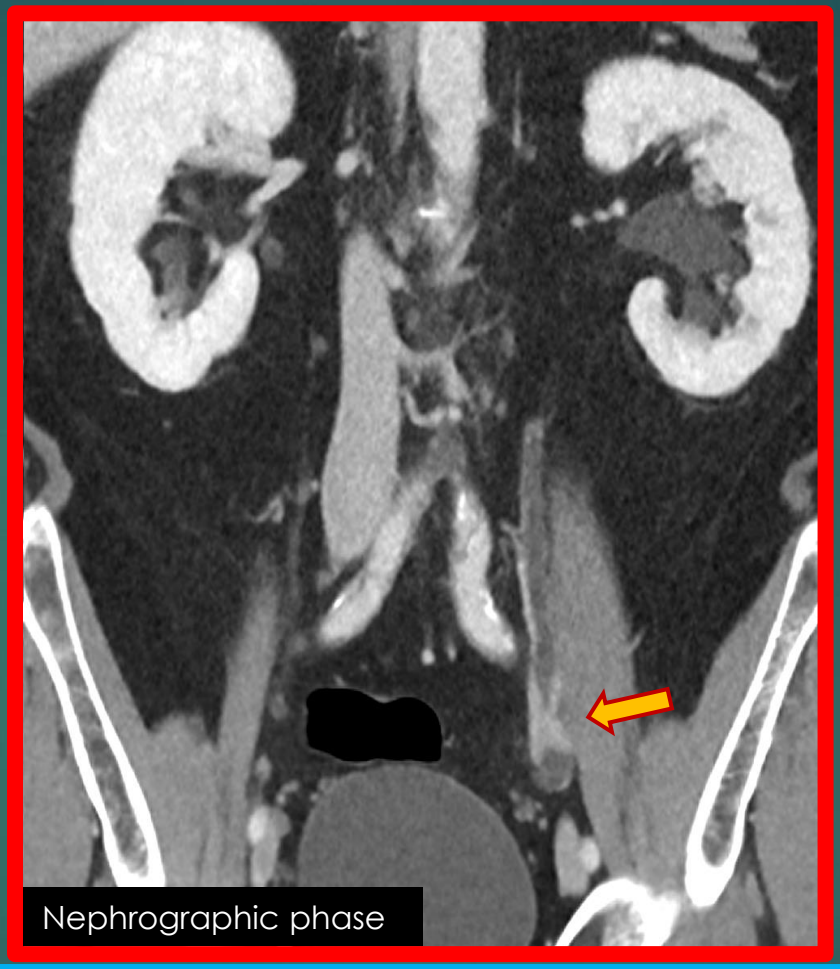
Control CT

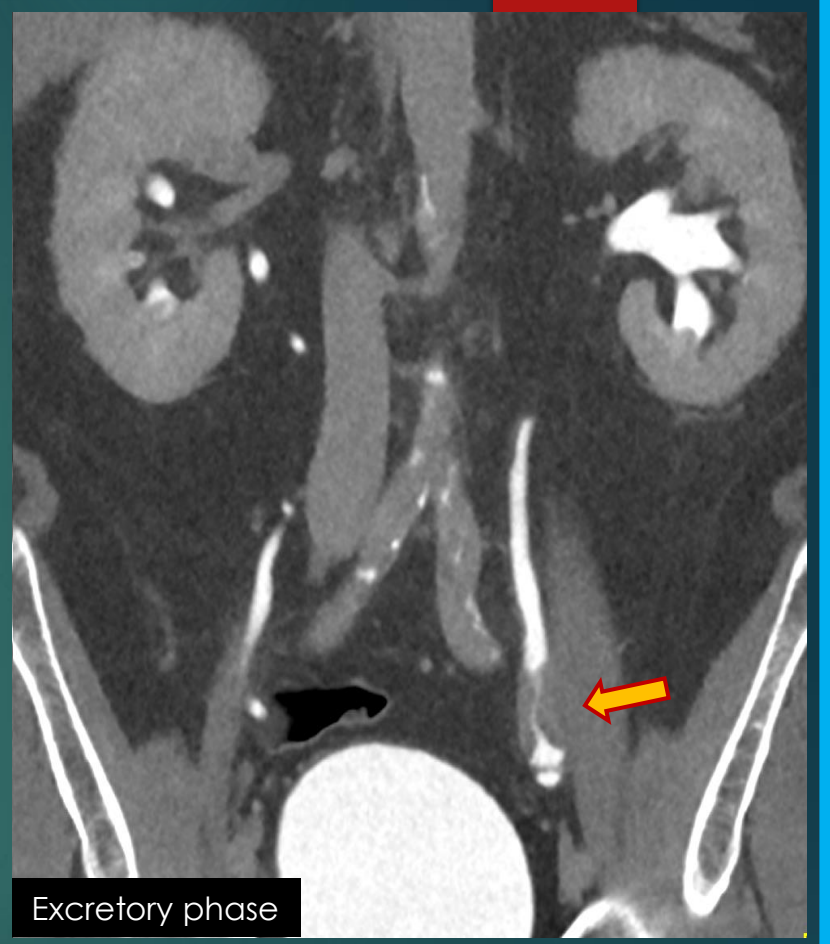
Experimental CT

Control CT

Experimental CT







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RESULTS

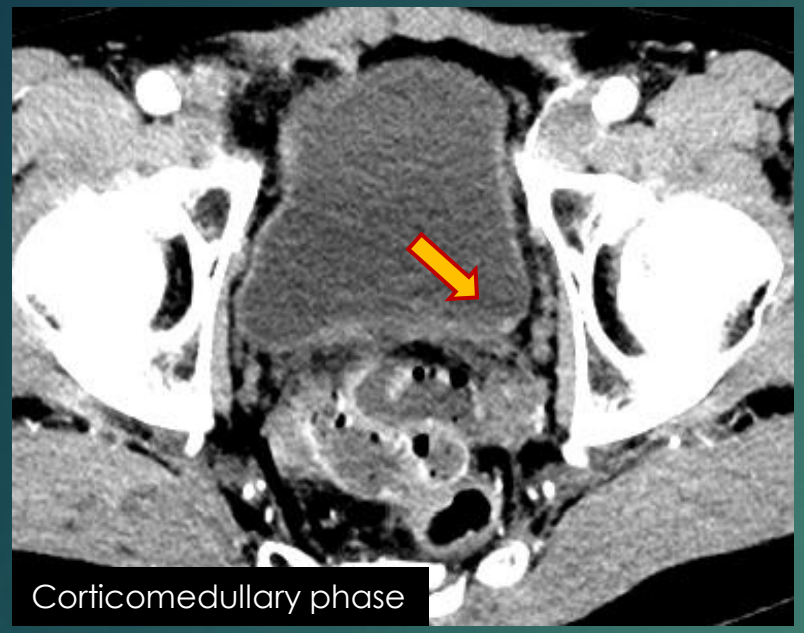
Upper Urinary Tract

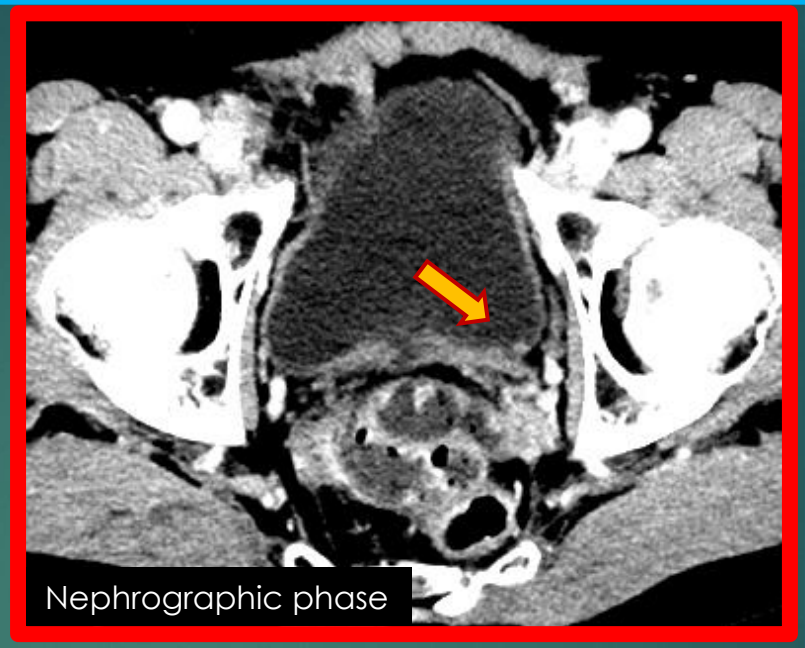
	Sensitivity (95% CI)	Specificity (95% CI)	NPV (95% CI)	PPV (95% CI)	Accuracy (95% CI)
Primary readers					
Control CT	80.0 (37.6-96.4)	98.0 (95.8-99.1)	99.7 (98.1-99.9)	40.0 (16.8-68.7)	97.7 (95.4-89.9)
Experimental CT	80.0 (37.6-96.4)	97.0 (94.5-98.4)	99.7 (98.1-99.9)	30.8 (12.7-57.6)	96.7 (94.1-98.2)
Difference	0.0 (-53.6 to 53.6)	1.0 (-1.9 to 4.0)	0.0 (-1.8 to 1.9)	9.2 (-30.9 to 47.7)	1.0 (-1.6 to 3.7)
Secondary readers					
Control CT	80.0 (37.6-96.4)	97.7 (95.3-98.9)	99.7 (98.1-99.9)	36.4 (15.2-64.6)	97.4 (95.0-98.7)
Experimental CT	80.0 (37.6-96.4)	97.7 (95.3-98.9)	99.7 (98.1-99.9)	36.4 (15.2-64.6)	97.4 (95.0-98.7)
Difference	0.0 (-53.6 to 53.6)	0.0 (-2.9 to 2.9)	0.0 (-1.8 to 1.8)	0.0 (-40.0 to 40.0)	0.0 (-2.7 to 2.7)

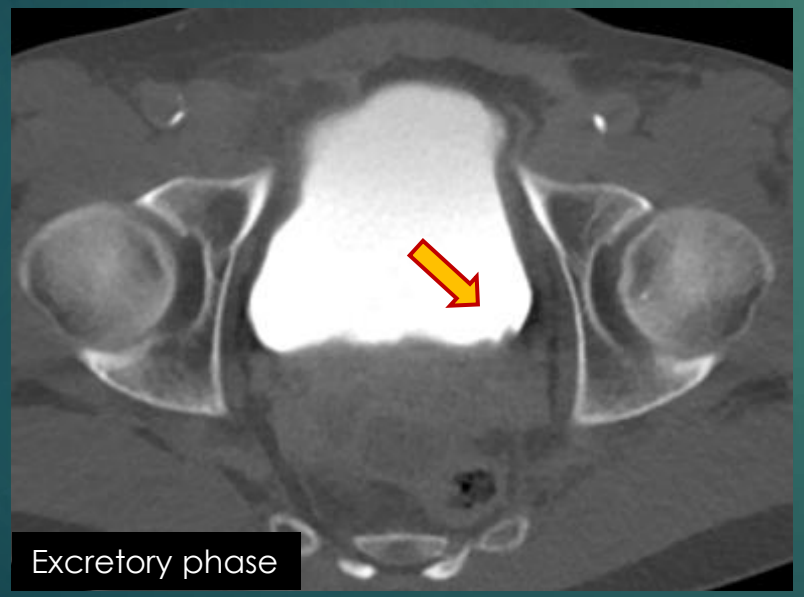
RESULTS

Bladder

	Sensitivity (95% CI)	Specificity (95% CI)	NPV (95% CI)	PPV (95% CI)	Accuracy (95% CI)
Primary readers					
Control CT	95.0 (83.5-98.6)	84.7 (79.9-88.5)	99.1 (96.9-99.8)	48.1 (37.4-58.9)	86.0 (81.7-89.5)
Experimental CT	92.5 (80.1-97.4)	83.6 (78.7-87.5)	98.7 (96.2-99.5)	45.7 (35.3-56.5)	84.7 (80.3-88.3)
Difference	2.5 (-11.8 to 17.1)	1.1 (-5.4 to 7.6)	0.4 (-2.3 to 3.3)	2.4 (-13.6 to 18.3)	1.3 (-3.3 to 5.9)
Secondary readers					
Control CT	82.5 (68.1-91.3)	92.9 (89.2-95.4)	97.3 (94.5-98.7)	63.5 (49.9-75.2)	91.5 (87.9-94.2)
Experimental CT	82.5 (68.1-91.3)	94.0 (90.5-96.3)	97.3 (94.5-98.7)	67.4 (53.4-78.9)	92.5 (89.0-95.0)
Difference	0.0 (-18.5 to 18.5)	-1.1 (-5.7 to 3.5)	0.0 (-3.4 to 3.4)	-3.9 (-22.9 to 15.7)	-1.0 (-4.7 to 2.7)

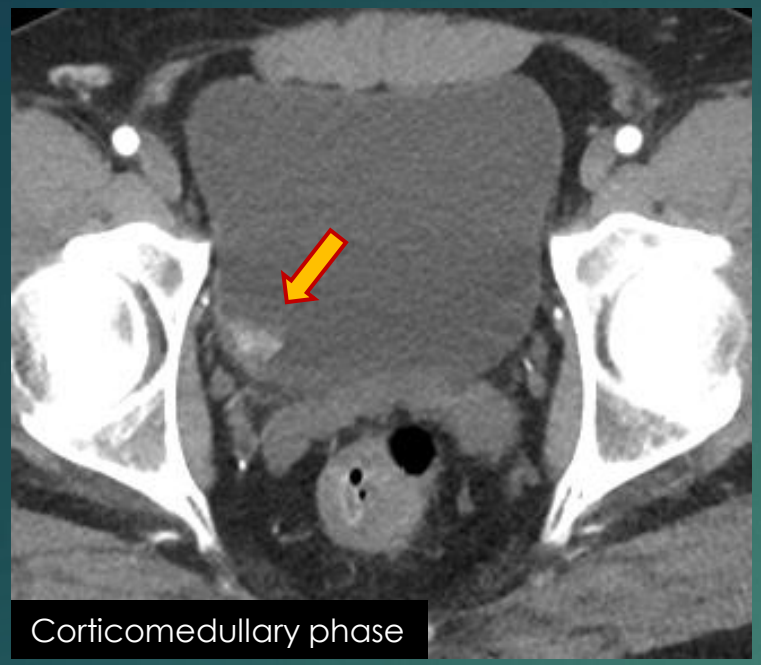


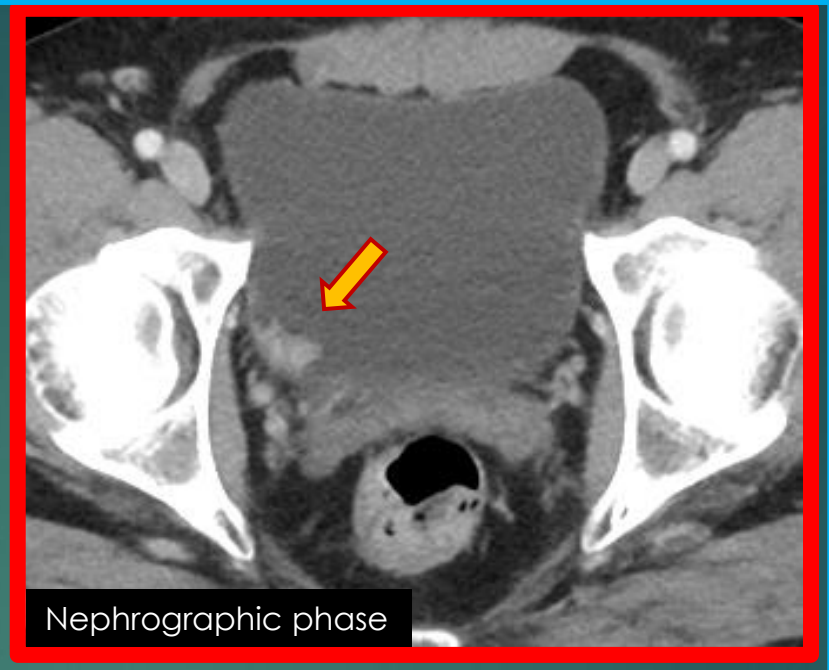


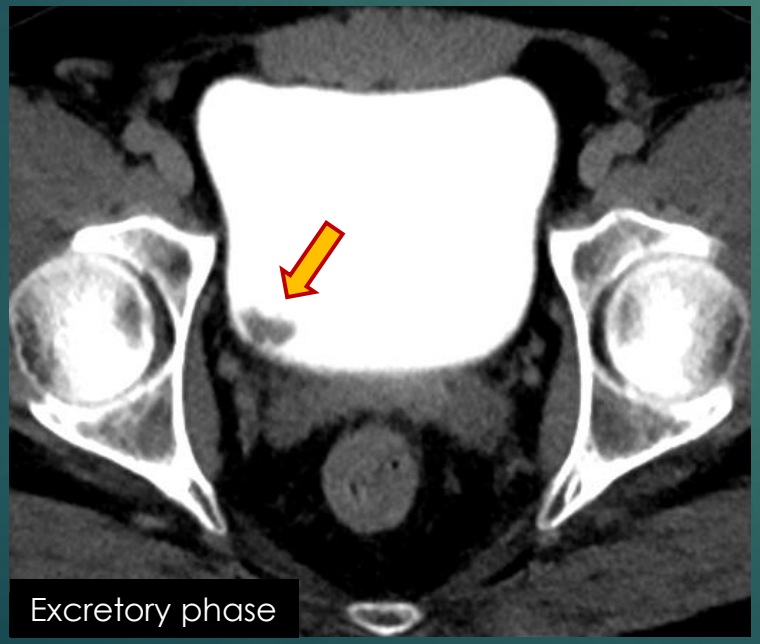


Control CT

Experimental CT







Control CT

Experimental CT

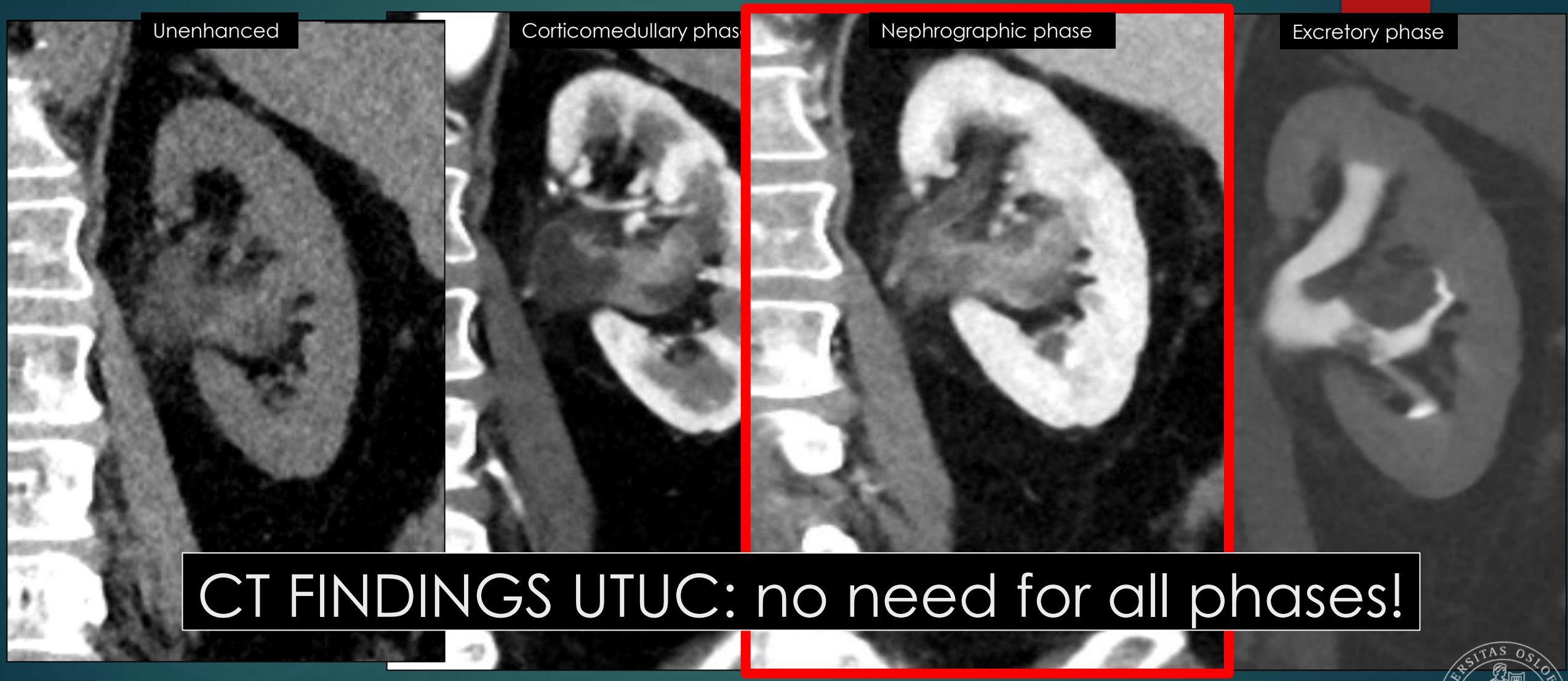
RESULTS

Bladder

	Sensitivity (95% CI)	Specificity (95% CI)	NPV (95% CI)	PPV (95% CI)	Accuracy (95% CI)
Primary readers					
Control CT	95.0 (83.5-98.6)	84.7 (79.9-88.5)	99.1 (96.9-99.8)	48.1 (37.4-58.9)	86.0 (81.7-89.5)
Experimental CT	92.5 (80.1-97.4)	83.6 (78.7-87.5)	98.7 (96.2-99.5)	45.7 (35.3-56.5)	84.7 (80.3-88.3)
Difference	2.5 (-11.8 to 17.1)	1.1 (-5.4 to 7.6)	0.4 (-2.3 to 3.3)	2.4 (-13.6 to 18.3)	1.3 (-3.3 to 5.9)
Secondary readers					
Control CT	82.5 (68.1-91.3)	92.9 (89.2-95.4)	97.3 (94.5-98.7)	63.5 (49.9-75.2)	91.5 (87.9-94.2)
Experimental CT	82.5 (68.1-91.3)	94.0 (90.5-96.3)	97.3 (94.5-98.7)	67.4 (53.4-78.9)	92.5 (89.0-95.0)
Difference	0.0 (-18.5 to 18.5)	-1.1 (-5.7 to 3.5)	0.0 (-3.4 to 3.4)	-3.9 (-22.9 to 15.7)	-1.0 (-4.7 to 2.7)

Conclusion

The accuracy of a single nephrographic phase CT is not inferior to the accuracy of a four-phase CT for detecting UC in patients with painless VH.



CT FINDINGS UTUC: no need for all phases!

Research question

Is a single nephrographic phase CT sufficient for detecting urothelial carcinoma (UC) in patients with painless visible hematuria (VH)?

Answer

YES!

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European Association of Urology

Urothelial Cancer

Is a Single Nephrographic Phase Computed Tomography Sufficient for Detecting Urothelial Carcinoma in Patients with Visible Haematuria? A Prospective Paired Noninferiority Comparison

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Abstract

Background: There is uncertainty about the utility of multiphase computed tomography (CT) compared with single-phase CT in the routine examination of patients with visible haematuria (VH).
Objective: To compare the accuracies of single nephrographic phase (NP) CT and four-phase CT in detecting urothelial carcinoma (UC).
Design, setting, and participants: This was a single-centre, prospective, paired, noninferiority study of patients with painless VH referred for CT before cystoscopy between September 2019 and June 2021. Patients were followed up for 1 yr to ascertain UC diagnosis.
Intervention: All patients underwent four-phase CT (control), from which single NP CT (experimental) was extracted. Both were independently assessed for UC.
Outcome measurements and statistical analysis: The primary outcome was the difference in accuracy between the control and experimental CT using a 7.5% noninferiority limit. Histologically verified UC defined a positive reference standard. Secondary outcomes included differences in sensitivity, specificity, negative (NPV) and positive (PPV) predictive values, and area under the curve (AUC). All results are reported per patient.
Results and limitations: Of the 308 patients included, UC was diagnosed in 45 (14.6%). The difference in accuracy between the control and experimental CT was 1.9% (95% confidence interval −2.8 to 6.7), demonstrating noninferiority. Sensitivity was 93.3% versus 91.1%, specificity was 83.7% versus 81.8%, NPV was 98.7% versus 98.2%, PPV was 49.4% versus 46.1%, and AUC was 0.96 versus 0.94 for the control versus experimental CT. Limitations included a low number of UC cases and no definite criteria for selecting a noninferiority limit.

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Takk for meg!

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