OSPEDALE SANDRO PERTINI

Dott. Egidio Sesti
Direttore Generale ff

LA CHIRURGIA UROLOGICA ROMANA 2010

VIII Corso di Aggiornamento
in Chirurgia Urologica
Corso Teorico-Pratico per Medici e Infermieri

Presidente
Prof. A. Panucci
Direttore
Prof. M. Schiavone

LA CHIRURGIA UROLOGICA ROMANA 2010

VIII CORSO DI AGGIORNAMENTO IN CHIRURGIA UROLOGICA

VIII SESSIONE

Le Neoplasie del Rene

Moderatore: A. Panucci

Nephron Sparing Surgery

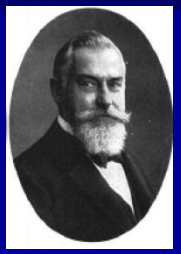
Carlo De Dominicis

NEPHRON SPARING SURGERY

Prof. C. De Dominicis
Dir. Cattedra di Urologia

Università “SAPIENZA” Roma

STORIA DELLA CHIRURGIA RENALE CONSERVATIVA



- 1887: Czerny eseguì la prima nefrectomia parziale per neoplasia
- 1937: Goldstein e Absehouse (34 casi)
- 1937-1950: Semb e Dufour (25 casi)
- 1947-1974: Puigvert (21 casi in elezione)
- 1950: Vermooten ***"small tumors and tumors of moderate size situated at one of the poles of the kidney, may be removed by partial resection out of necessity, but was contraindicated if the opposite kidney was healthy"***
- 1980: sviluppo della nefrectomia parziale in elezione, in base alle evidenze di buon controllo oncologico

Razionale: studi anatomo-patologici

- Da studi autoptici: piccoli tumori renali scarsamente metastatici (< 7% in RCC < 5cm, Bell 1938)
- Alla microscopia ottica: tessuto adiacente libero da tumore entro 1 cm
- 16-23% lesioni benigne (oncocitoma, angiomiolipoma, adenoma metanefrico, cisti emorragica)

Bell, Shakeen, Hale, Burkland, Kozall and Kirshbaum

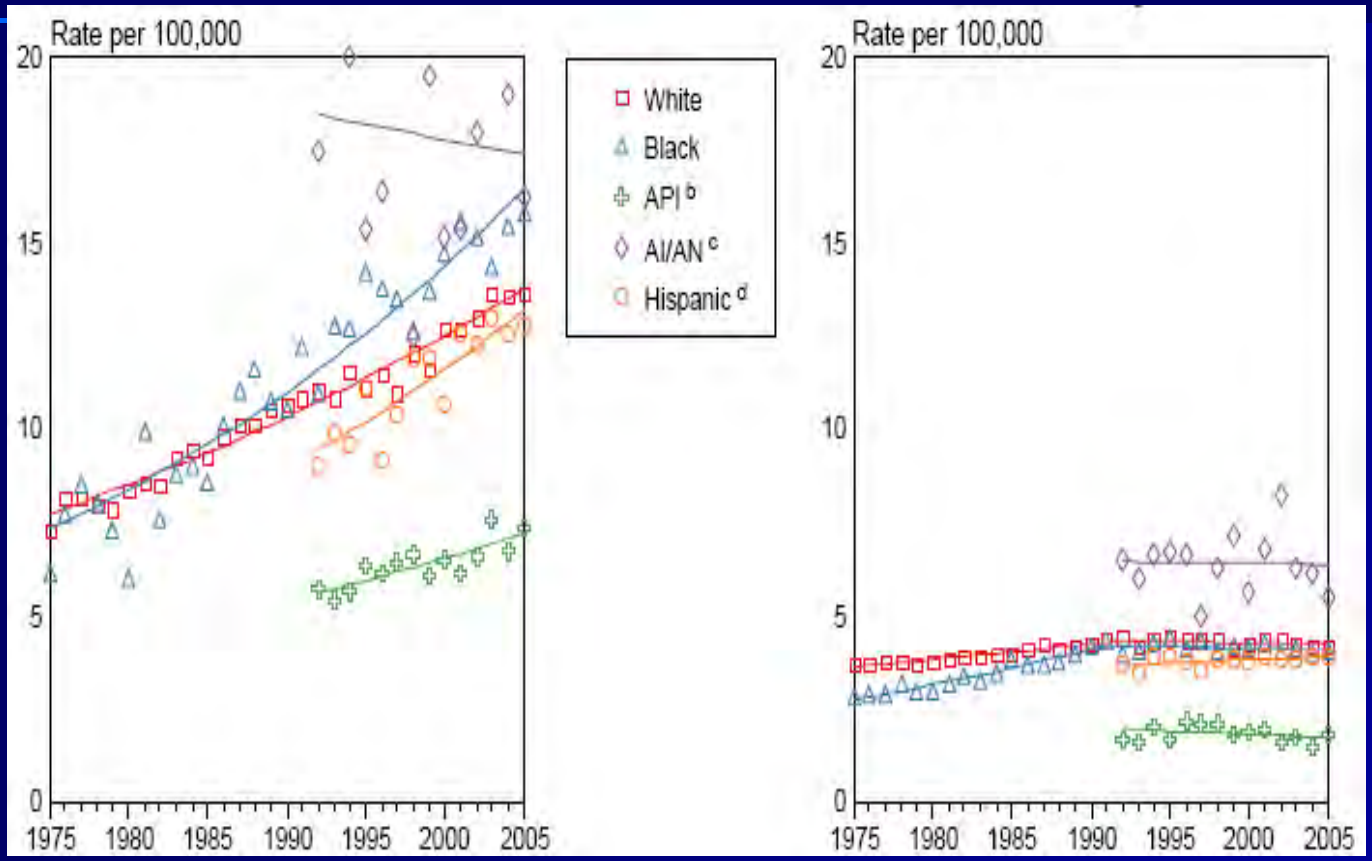
Razionale: oncologico

- RCC origina dalla corticale
- In genere localizzato
- Modalità di crescita espansiva
- Circondato da una pseudocapsula
- Raramente invade le strutture circostanti

NSS: perchè ci interessa tanto?

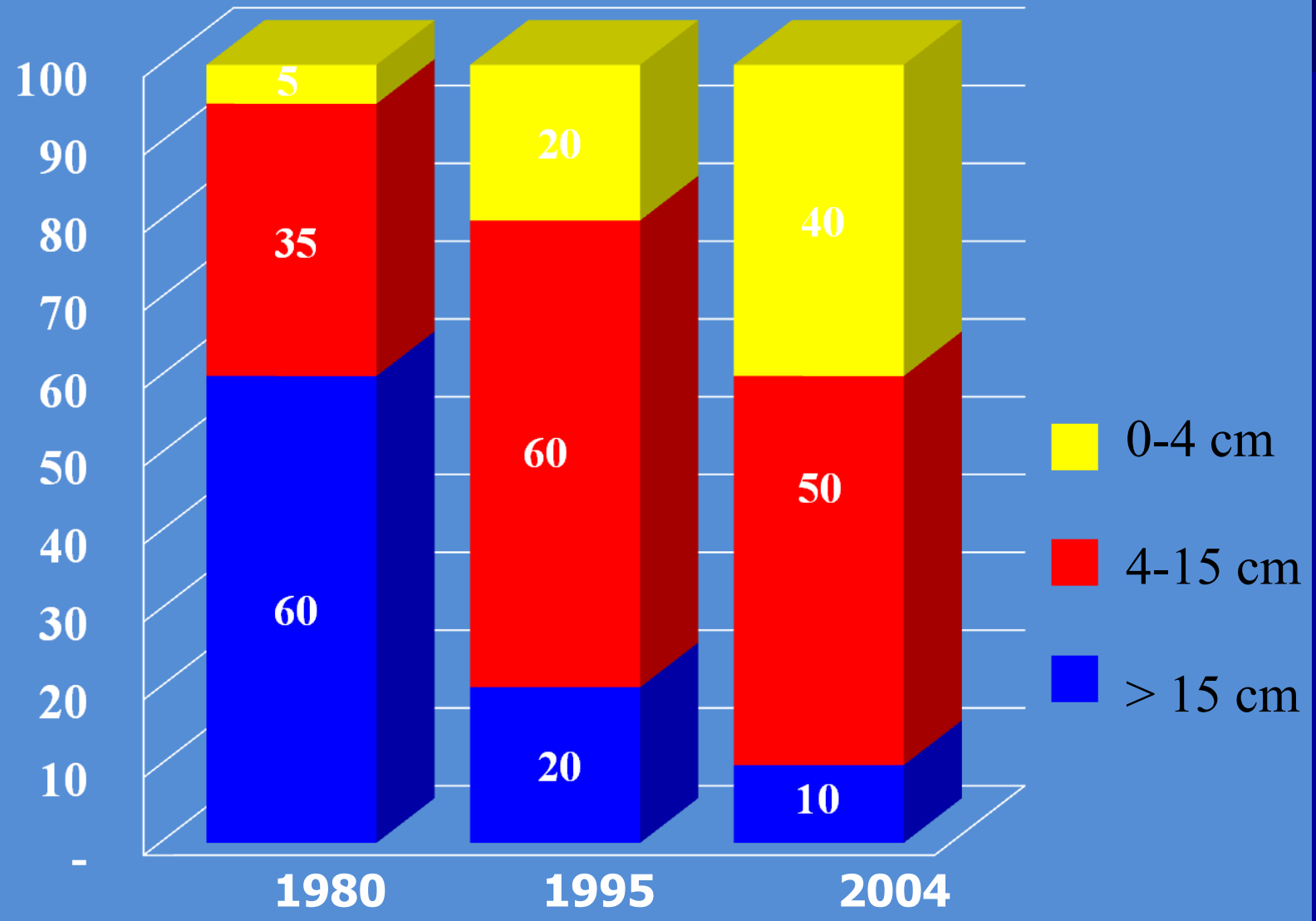
INCIDENCE

MORTALITY

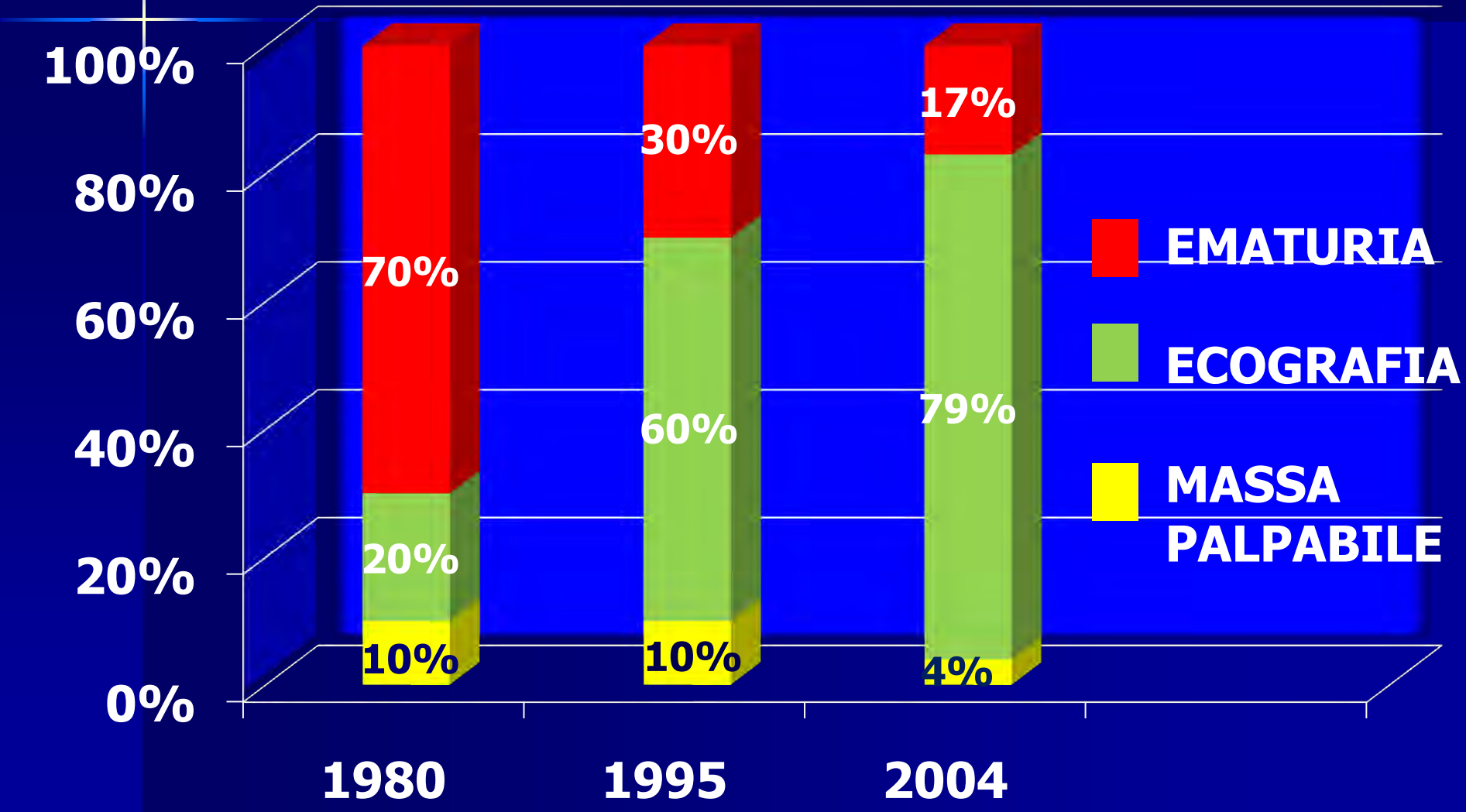


da *SEER Cancer Statistics Review 1975-2005, NCI*

Dimensioni del tumore



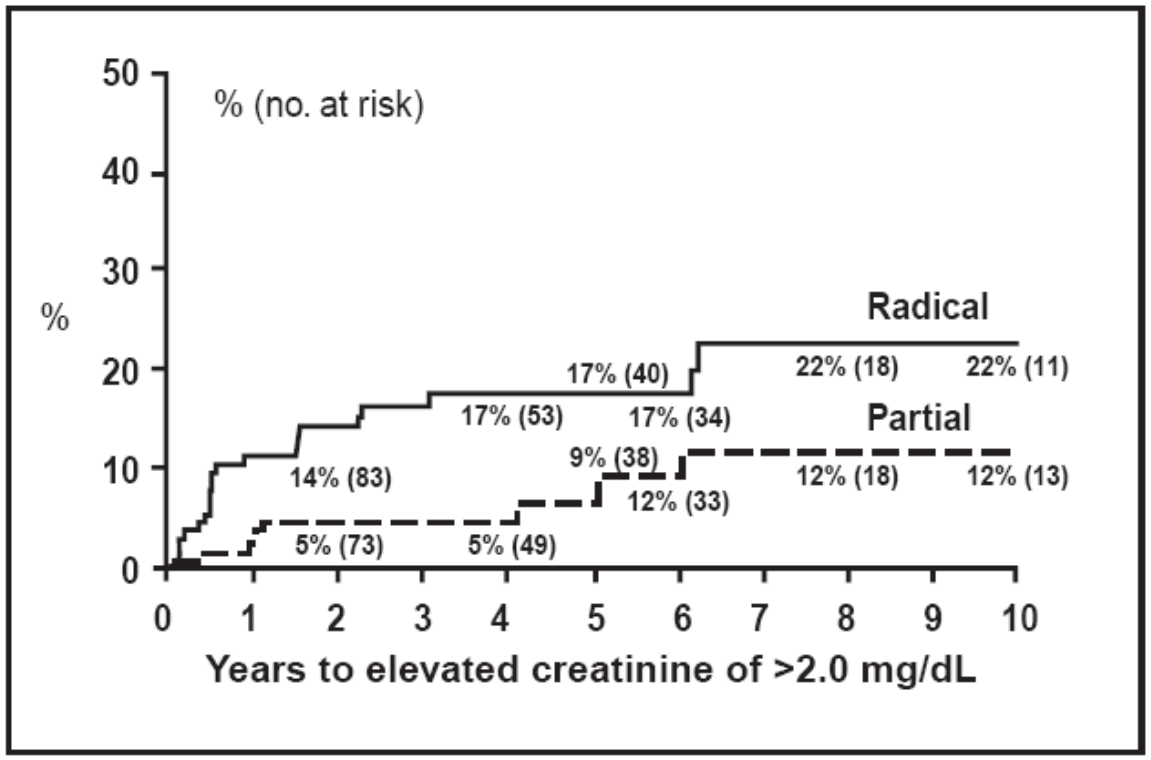
Presentazione alla diagnosi



Funzionalità renale

Matched Comparison of Radical Nephrectomy vs Nephron-Sparing Surgery in Patients With Unilateral Renal Cell Carcinoma and a Normal Contralateral Kidney

Weber K. O. Lau, MD; Michael L. Blute, MD; Amy L. Weaver, MS; Vicente E. Torres, MD, PhD; and Horst Zincke, MD, PhD



IRC a 10 anni molto più frequente dopo RN (22.4% vs 11.6%). Rapida tendenza a sviluppare IRC

Chronic kidney disease after nephrectomy in patients with renal cortical tumours: a retrospective cohort study

William C Huang, Andrew S Levey, Angel M Serio, Mark Snyder, Andrew J Vickers, Ganesh V Raj, Peter T Scardino, and Paul Russo

Chronic Kidney Disease (CKD): GFR < 60 ml/m/1.73m^2

Follow-up 3 anni (662 pts)	NSS	Nefrectomia Radicale
Sopravvivenza libera da CKD	80%	35%

Radical Nephrectomy indipendent risk factor for CKD

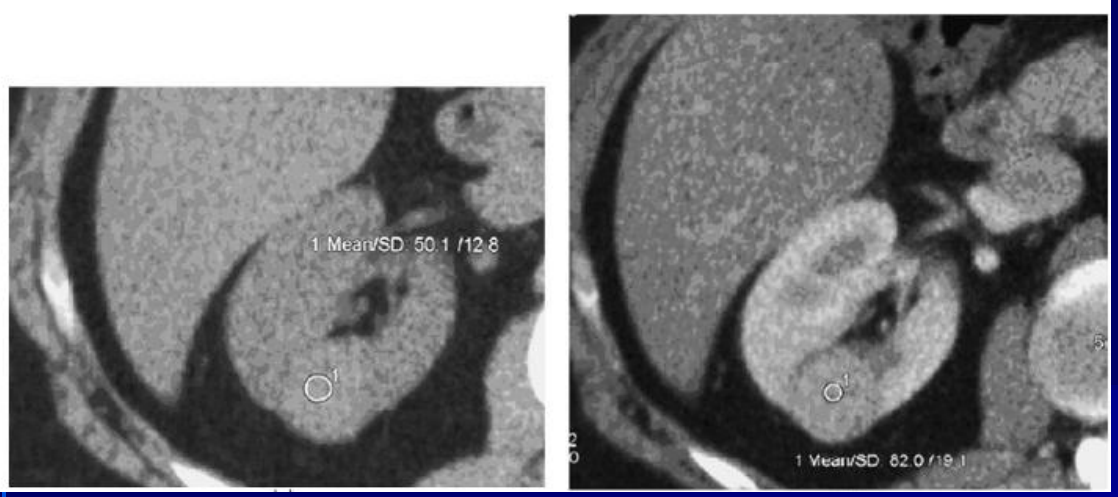
Huang AC, Lancet 2006

Indicazioni NSS

- Assolute
  - Bilateral RCC
  - RCC in rene unico
- Relative
  - RCC monolaterale ma con rene controlaterale di ridotta funzionalità (Calcolosi, pielonefrite, diabete, nefroscelrosi)
  - RCC in von Hippel Lindau disease (VHL)
- Elettive
  - RCC < 4 cm e normale rene controlaterale
  - 4 > RCC < 7 dati preliminari

Valutazione pre-operatoria

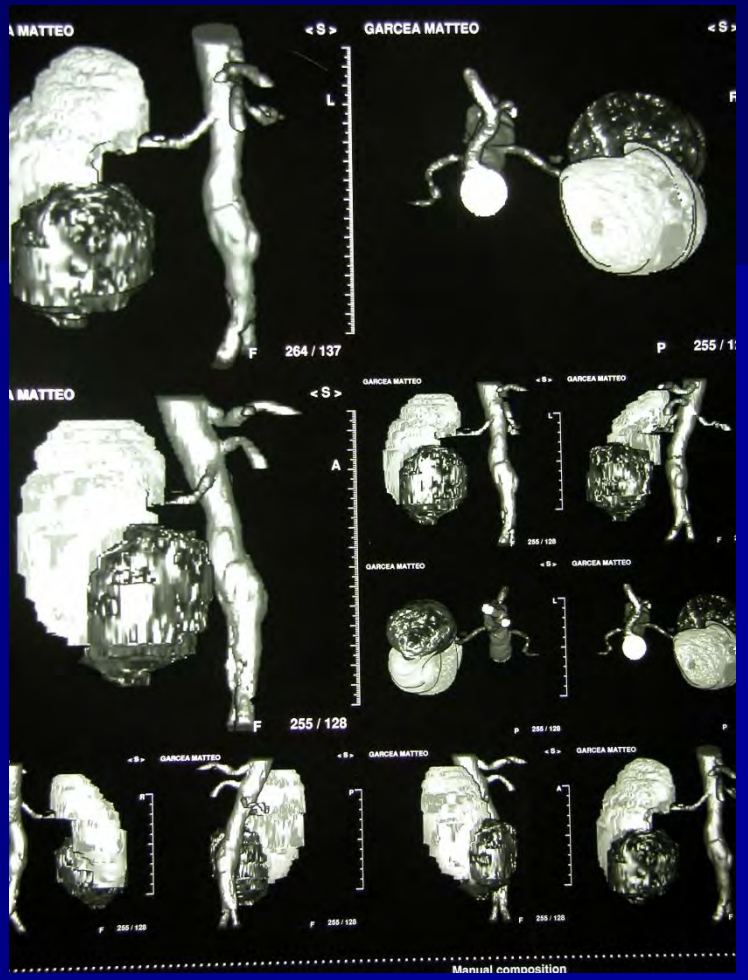
- Anamnesi ed esame obiettivo
- Creatinemia, funzionalità epatica e proteinuria
- Rx Torace
- 3D TC
  - Fase angiografica
  - Venografica
  - Urografica



a b

c

RCC del rene destro studiato in differenti fasi con TC seriale: (a) senza mezzo di contrasto; (b) fase corticomidollare; (c) fase nefrografica.



RCC destro con ricostruzione 3-D: evidenziati i rapporti tra la massa, il rene e la via escretrice

TECNICA CHIRURGICA

- NEFRECTOMIA PARZIALE
  - rimozione del tumore con 1-2 cm di tessuto sano circostante

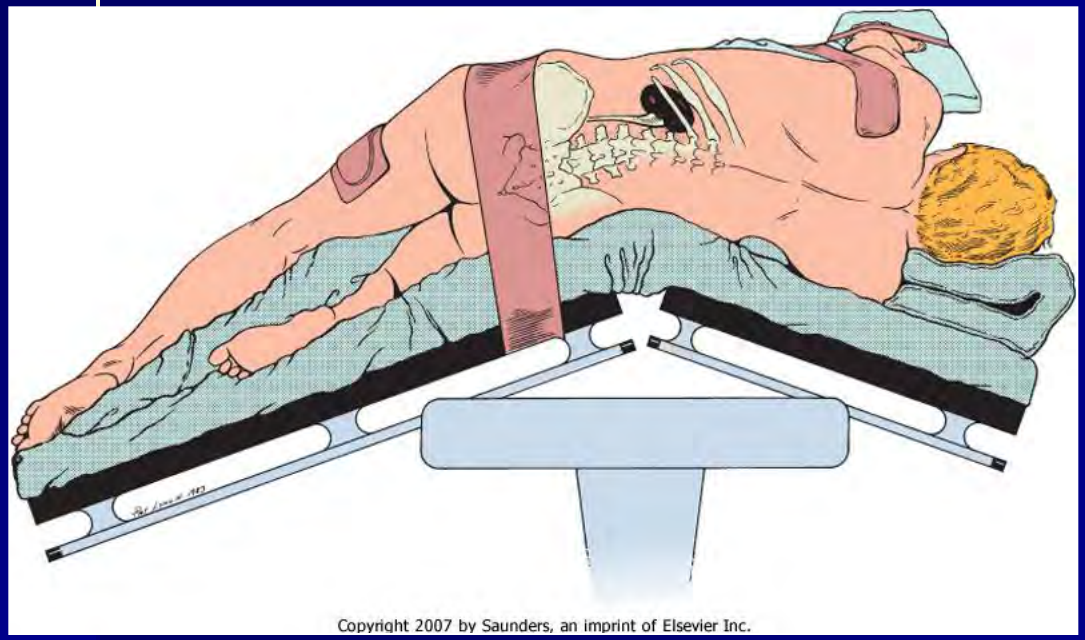
- ENUCLEAZIONE TUMORALE
  - Resezione del tumore con la sua pseudocapsula e un sottile strato di parenchima (2 mm)

gestione operatoria del paziente

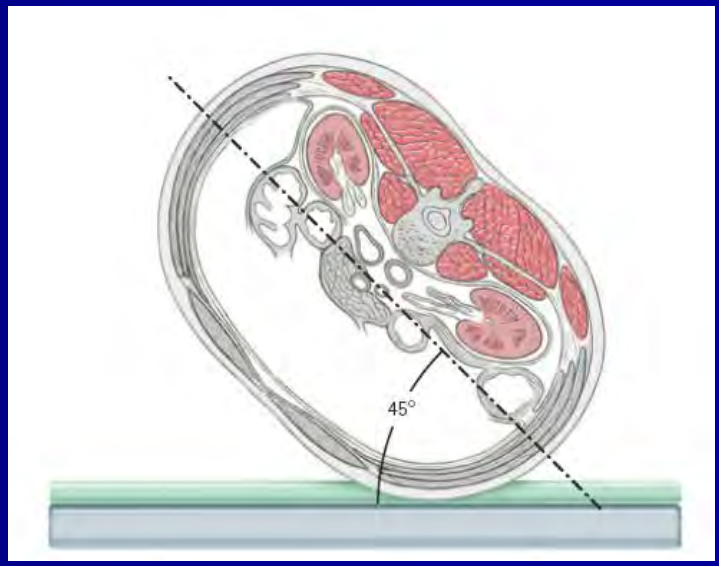
Abbondante idratazione pre-operatoria e intraoperatoria

Somministrazione intraoperatoria di mannitolo

Dettagli di tecnica: accesso *open*



Incisione obliqua a livello dell' XI-X costa



-buon accesso al parenchima,al peduncolo vascolare e al sistema collettore
-no contaminazione del peritoneo
-possibilità di modificare e ampliare l' incisione

Ischemia intraoperatoria

- In funzione della sede e delle dimensioni della neoplasia
- Occlusione temporanea dell' arteria renale (ischemia calda)

VANTAGGI:

- diminuzione del sanguinamento intraoperatorio
- riduzione del turgore parenchimale
- migliore accesso alle strutture intrarenali

Assessing the Impact of Ischaemia Time During Partial Nephrectomy

Study	Subject matter	*n*	Mean ischaemia time	Mean tumour size	Comments
OPN					
Fergany et al [42]	OPN in solitary kidneys	400	38.1 min	4.18 cm	Renal function quantified by sCR Satisfactory long-term renal function: no increase of sCR in 21%, only minor increase in 41%; increase of sCR >50% of preoperative value in 38%; 14% permanent dialysis Significant factors for postoperative renal function: age, size of resected parenchyma, time interval after contralateral nephrectomy
Ghavamian et al [43]	OPN in solitary kidneys	76	NA	4.8 cm	Late renal insufficiency in 12.7%; acute renal failure in 12.7% Renal insufficiency declared as sCR >2.0 mg/dl 12.7% ex vivo resection
Iida et al [44]	Effect of CI (ice slush) on renal function after OPN; 3 groups (<30 min, 30–60 min, and >60 min CI)	131	NA	2.8 vs 2.9 vs 3.9 cm	Renal function compared by eGFR (pre- and >12 mo postoperatively) Cutoff time for significantly higher late-stage CKD in CI was 44 min Other risk factors for late-stage CKD: operation time, imperative indication, preoperatively elevated eGFR, age
Thompson et al [45]	Multicentric study on impact of ischaemia time in solitary kidneys	537	NA	2.0 vs 3.5 vs 4.0 cm (*n* = 85 no ischaemia; *n* = 174 WI; *n* = 278 CI)	CI performed by ice slush; sCR measurement Higher complication rate after clamping (WI and CI) Higher incidence of acute renal failure in WI >20 min or CI >35 min WI >20 min resulted in increased risk of renal insufficiency and permanent dialysis
Yossepowitch et al [46]	Description of GFR course after OPN in solitary and/or healthy contralateral kidneys	662	35 vs 31 min (two functioning kidneys vs solitary kidney)	2.5 vs 3.5 cm (two functioning kidneys vs solitary kidney)	GFR measurement: preoperative, 1 and 12 mo postoperative Length of CI time determines short-term postoperative GFR (particularly in solitary kidneys) Long-term GFR seems to be unaffected by ischaemia time
LPN					
Abukora et al [47]	Renal function comparison of 12 WI patients vs 14 CI patients after LPN	26	31.5 vs 44.5 min	2.31 vs 2.16 cm	No difference in postoperative MAG3 renal function tests up to 6 mo after both procedures No significant mean renal function loss after both procedures CI by cold arterial perfusion
Bhayani et al [48]	Renal function after LPN (without ischaemia [*n* = 42], WI <30 min [*n* = 48], and WI >30 min [*n* = 28])	118	0 vs <30 min vs >30 min (max 55 min)	2.4 vs 2.5 vs 2.8 cm	No statistically significant difference in sCR increase (+0.05 vs +0.06 vs +0.08 mg/dl) in all groups; no renal insufficiency; no permanent dialysis WI up to 55 min has no influence on long-term renal function (median: 28 mo)
Desai et al [49]	Comparison of LPN (WI <30 min [*n* = 74] or WI >30 min [*n* = 105])	179	31 min (22 vs 37 min)	2.9 cm (2.8 vs 3.1 cm)	Measured by MAG3 before and 1 mo after surgery Data suggest that clinical sequelae are minimal in WI <30 min WI >30 min, especially in advancing age and preexisting renal insufficiency, is associated with greater ischemic renal dysfunction Recovery of renal function is delayed the longer WI is required
Foyil et al [50]	Comparison of LPN (without ischaemia, WI, and CI) by long-term CrCl change	98	0 vs 27 min (WI) vs 38 min (CI)	2.4 vs 3.1 (WI) vs 2.9 cm (CI)	Measurement of CrCl (Cockcroft-Gault) Direct correlation between time of ischaemia and degree of acute renal damage Safe WI time before permanent renal damage was <45 min
Lane and Gill [51]	5-yr outcome after LPN	557	NA	2.9 cm	Mean sCR elevation from 0.9 to 1.0 mg/dl 4.1% abnormal postoperative renal function 2.0% CKD; 1.8% kidney loss
Porpiglia et al [52]	Prospective study analyzing renal function after WI >30 min	18	39.0 min (WI)	3.4 cm	Measurement of sCR, eGFR, and MAG3 within first postoperative year Recommendation: keep WI within 30 min to avoid partial renal damage
Shekarriz et al [53]	Prospective study describing postoperative renal function (MAG3)	17	22.5 min (WI)	3.0 cm	MAG3 and GFR follow-up until 3 mo postoperatively No significant negative association between clamping time and renal function change Clamping up to 44 min WI acceptable

CI = cold ischaemia; CKD = chronic kidney disease; CrCl = creatinine clearance; eGFR = estimated glomerular filtration rate; GFR = glomerular filtration rate; LPN = laparoscopic partial nephrectomy; MAG-3 = mercaptoacetyltriglycine; OPN = open partial nephrectomy; SCR = serum creatinine rate; WI = warm ischaemia.

EUROPEAN UROLOGY 56 (2009) 625–635

NSS: tempo ischemia e funzionalità renale

537 pts con rene unico

Tempo Ischemia calda	Risk CKD	Incremento Creatinemia > 0.5 mg/dl	Dialisi
T< 20 minuti	19%	15%	4%
T > 20 minuti	41%*	42%*	10%*

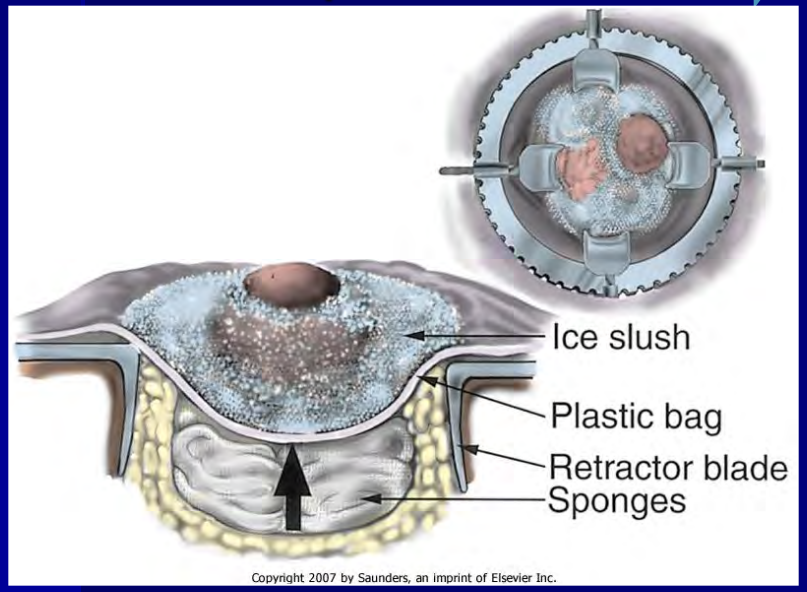
* p< 0.001

Chronic Kidney Disease (CKD): GFR < 60 ml/m/1.73m^2

Thompson RH, J Urology 2007

Ischemia a freddo

1. occlusione dell’ arteria renale
2. il rene viene completamente circondato con un telo impermiabile su cui è posizionato ghiaccio sterile sfuso
3. dopo 10-15 min ➡ temperatura 20°C



TEMPO DI ISCHEMIA CIRCA 3 ORE

Meccanismi del danno renale da ischemia

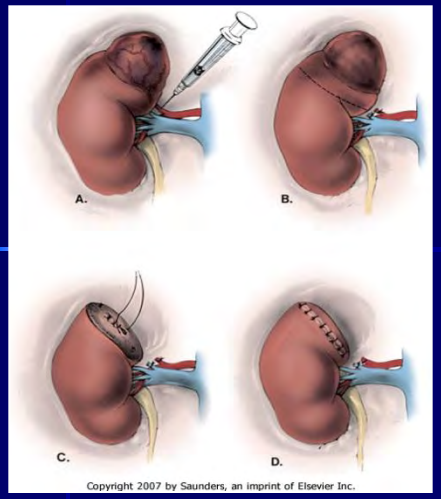
- ↑ livelli locali di angiotensina II, trombossani, leucotrieni, endotelina I, adenosina) ➡ persistente vasocostrizione
- attivazione della cascata coagulativa
- ↑ interazione endotelio-leucociti, rilascio citochine, interazioni endotelio-piastrine ➡ trombosi dei piccoli vasi ➡ necrosi tubulare

- danno da riperfusione

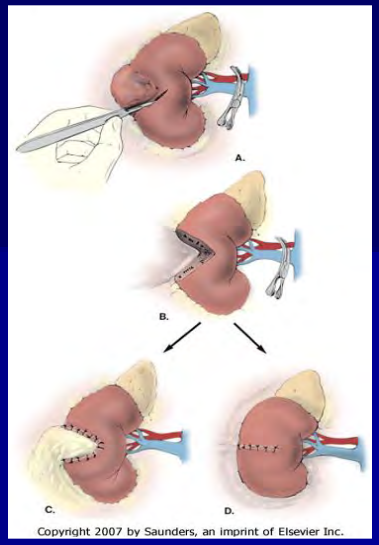
Nefrectomia parziale:

- nefrectomia polare
- resezione a cuneo
- resezione trasversale estesa

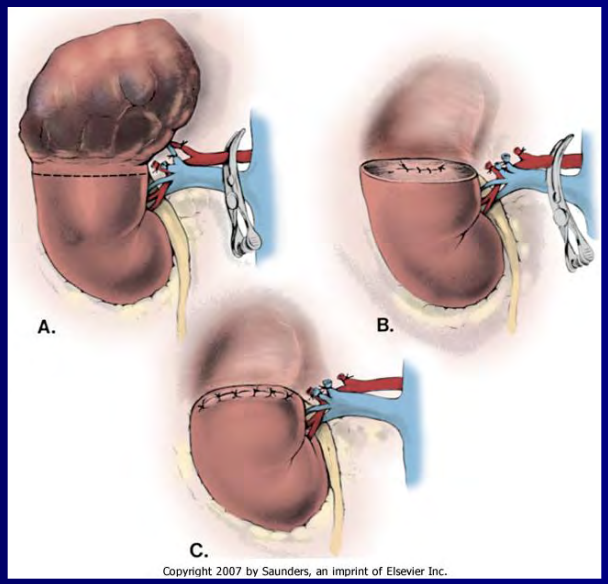
Nefrectomia polare



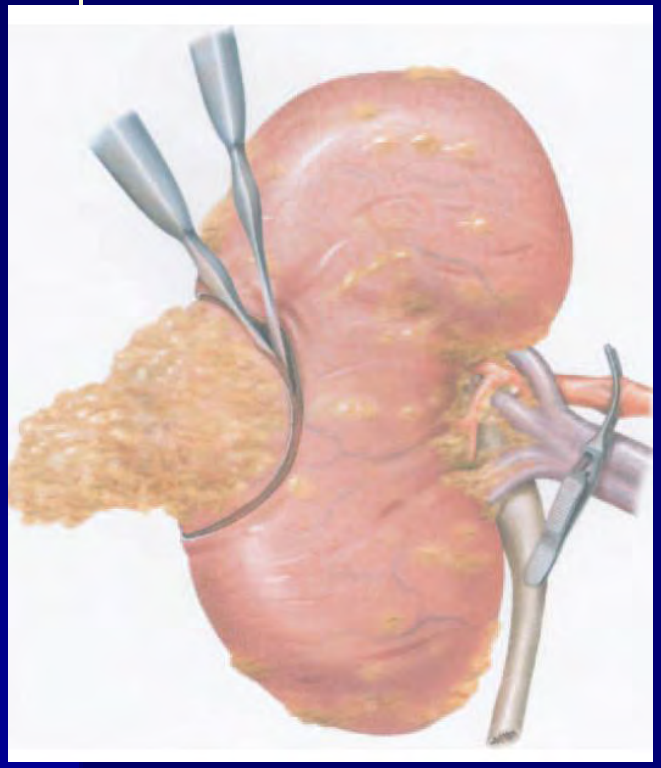
Resezione a cuneo

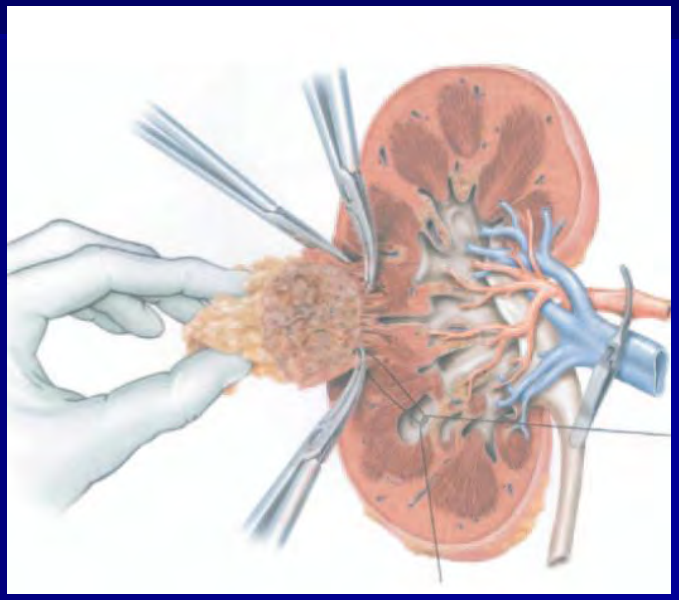


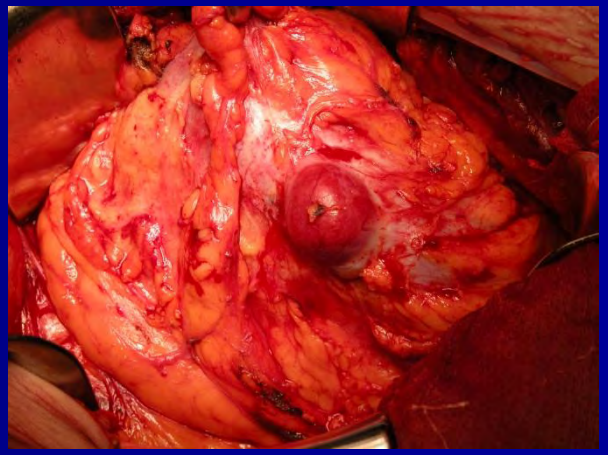
Resezione trasversale estesa

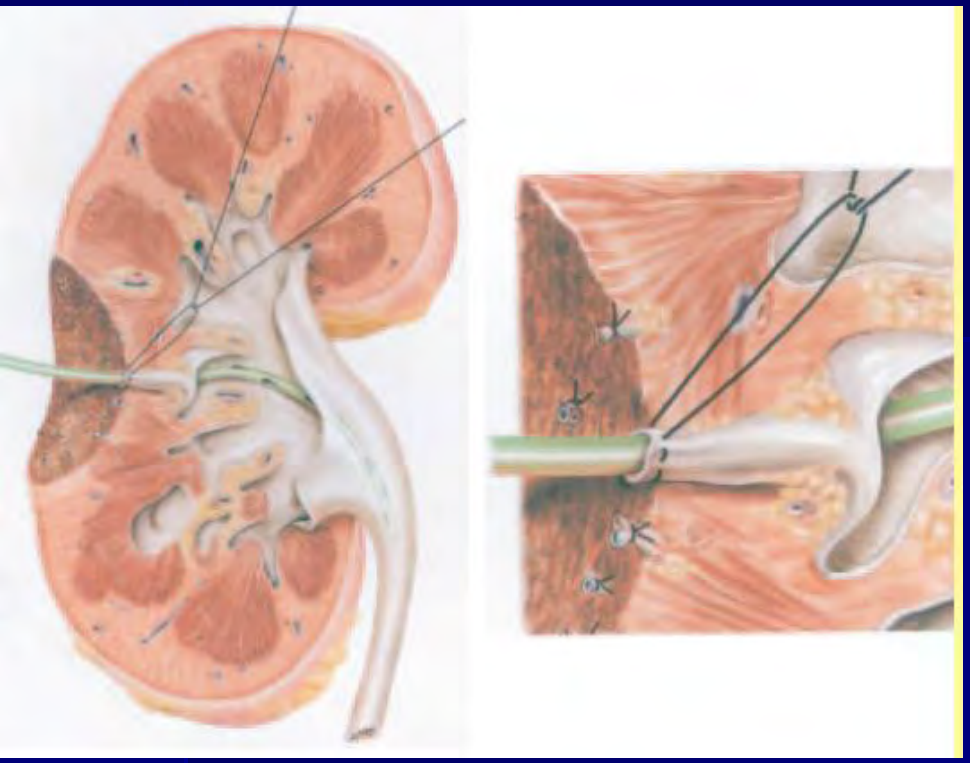


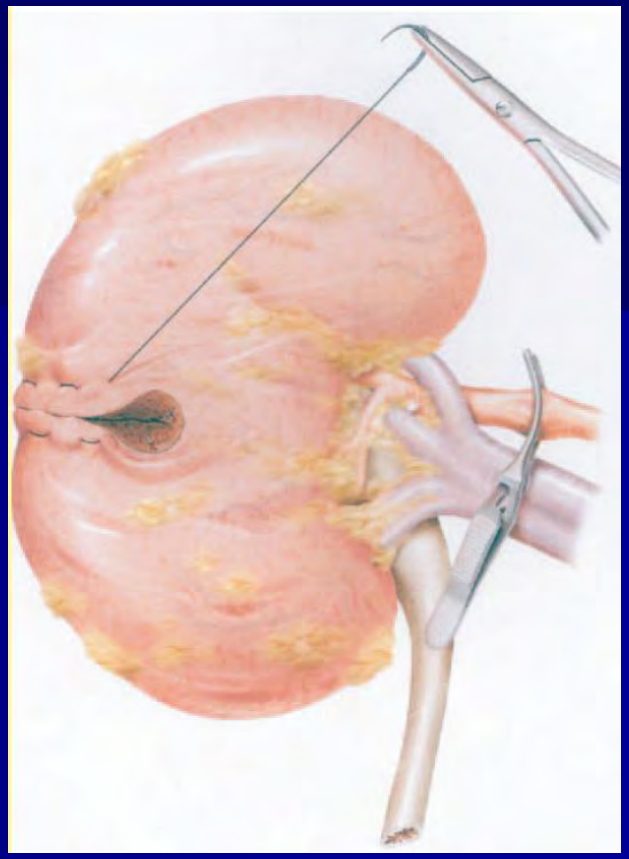
Enucleoresezione

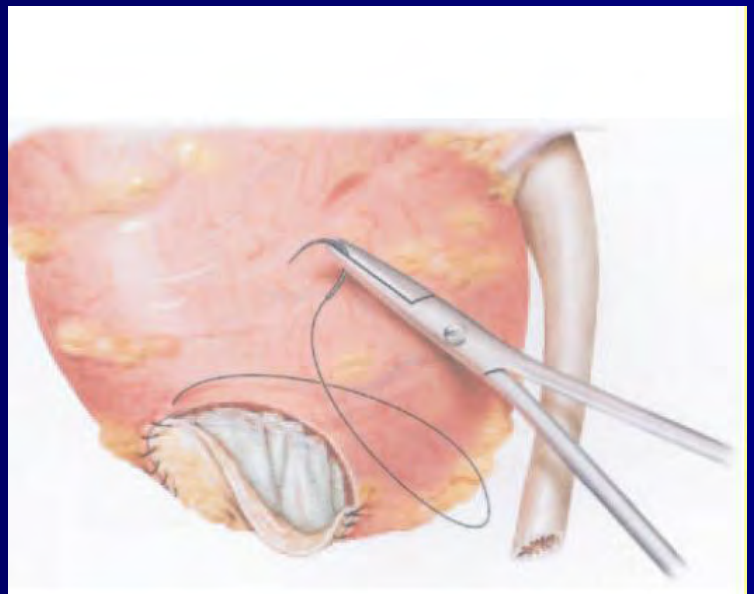


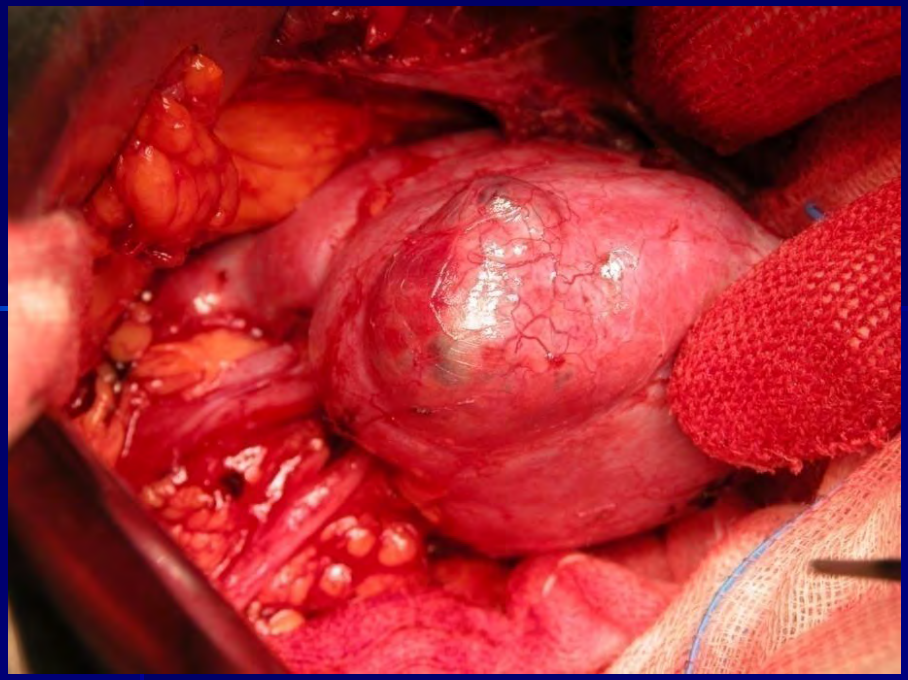






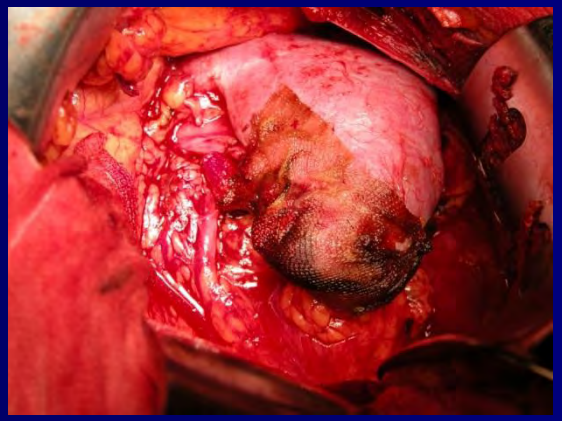


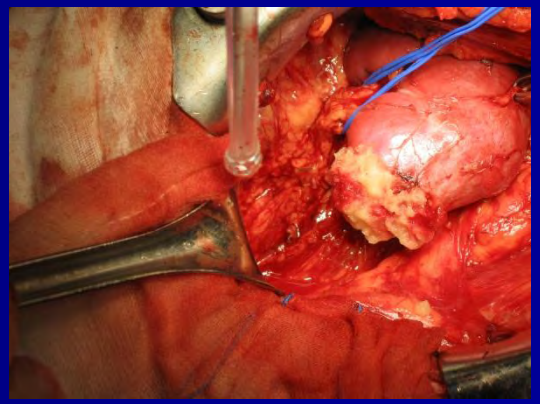




NSS
Tecniche di emostasi

- Colle emostatiche
  - FloSeal (Gel matrix thrombin)
  - Tachosil (Equin collagen patch and fibrine glue, human fibrinogen and thrombin)
  - Tisseel (Fibrin Gel)
  - Bioglue (Bovine Serum Albumin)
  - Glubran (Cyanocrylate Glue)
  - Surgicel (Oxidized regerated Cellulose)





NSS
Tecniche di emostasi

- Dissettori/bisturi emostatici
  - Tissue-Link (Monopolar saline cooled radiofrequency device)
  - Laser 80 W KTP (Potassium titanyl phospate)
  - Helix Hydro jet ERB (Water jet dissection)
  - MTC (Microwave tissue coagulator)
  - Bisturi Argon

COMPLICANZE

- **Fistola urinaria: 1.4 – 17.4 %**
- **Emorragia intraoperatoria: 1.2–4.5 %**
- **Emorragia postoperatoria: 0 – 4.5 %**
- **Reintervento a cielo aperto: 0 – 5.5 %**
- **Insufficienza renale acuta: 0 – 26 %**

J Urol 2004, Eur Urol 2006, Eur Urol 2007

Risultati open nss

Follow-up	pts	Tumore (cm)	Cancer Survival %	Recidiva distanza %	Recidiva locale %
5 Anni	1229	2,7 - 4,1	92 – 98	1,8 – 17	0 - 7,3
10 anni	958	3 - 4,7	73 - 97	2,8 - 17	2,3 - 10

Lane BR and Novick AC, BJU 2007

NSS in elezione:l' attuale cut-off (4 cm) è ampliabile alla luce delle nuove esperienze?

Group No.	No. Local Recurrence	No. Metastatic Disease	No. Local Recurrence + Metastatic Disease	Total No. (%)	% 5-Yr. Survival	% 10-Yr. Survival
1	0	3	0	3 (2)	99	94
2	3	7	2	12 (7)	98	91
3	3	12	2	17 (13.5)	88	71
4	2	6	4	12 (25)	82	62

Hafez KS, et al J Urol 1999;162:1930–3.

Combinando insieme i gruppi 1-2 e il gruppi 3-4, la differenza appare significativa in termini di ricorrenza di malattia (p=0.001),e di sopravvivenza a 5 e 10 anni (p=0.03)

gruppo 1: diametro ≤ 2.5 cm
gruppo 2: diametro compreso tra 2.5 e 4 cm
gruppo 3: diametro maggiore di 4 cm e fino a 7 cm
gruppo 4: diametro maggiore di 7 cm

il risultato è attribuibile alla tecnica chirurgica?

1) i pazienti con migliore outcome, cioè quelli con RCC≤ 4 cm, sono confrontati con un gruppo comprendente non solo RCC > 4 cm, ma anche maggiori di 7 cm
2) mancanza di un gruppo di controllo sottoposto a nefrectomia radicale per le stesse indicazioni

Efficacia della NSS per RCC > 4 cm

TABLE 3. *Analysis of type of recurrence according to tumor size and type of surgery*

	No. T1a Tumors (%)	No. T1b Tumors (%)
No. partial nephrectomy (p = 0.2):		
No recurrence	119 (96.8)	25 (89.3)
Local recurrence	1 (0.8)	1 (3.6)
Distant recurrence	3 (2.4)	2 (7.1)
No. radical nephrectomy (p = 0.001):		
No recurrence	166 (94.8)	179 (82.1)
Local recurrence	1 (0.6)	5 (2.3)
Distant recurrence	8 (4.6)	34 (15.6)
p Value	0.6 (not significant)	0.5 (not significant)

(2004, Patard et al.)

la nefrectomia radicale non migliora l'outcome dei pazienti in stadio T1b

Table 5 – Comparison of 550 elective nephron-sparing surgical procedures for oncologic results according to tumour size

	Tumours ≤4 cm	Tumours >4 cm	*p*
Positive margins (*n* = 542)	7 (1.5%)	1 (1.3%)	0.9
Margin size, mm ± SD (*n* = 148)	4.2 ± 3.7	5.3 ± 4.9	0.2
Local recurrence (*n* = 520)	4 (0.9%)	1 (1.3%)	0.7
Distant recurrence (*n* = 506)	7 (1.6%)	3 (3.9%)	0.2
Deaths (*n* = 500)	20 (4.7%)	7 (9.3%)	0.1
Cancer-related deaths (*n* = 498)	9 (2.1%)	2 (2.7%)	0.8

(2007, Patard et al.)

è importante separare le indicazioni assolute da quelle elettive alla NSS

i pz candidati imperativamente a NSS hanno spesso tumori molto grandi e performance status scadente (fattore prognostico)

Positività dei margini chirurgici post- OPN: 0.8-6.8%

(Thompson 2005, Sutherland 2002, Porpiglia 2008)

Positive Surgical Margin Appears to Have Negligible Impact on Survival of Renal Cell Carcinomas Treated by Nephron-Sparing Surgery

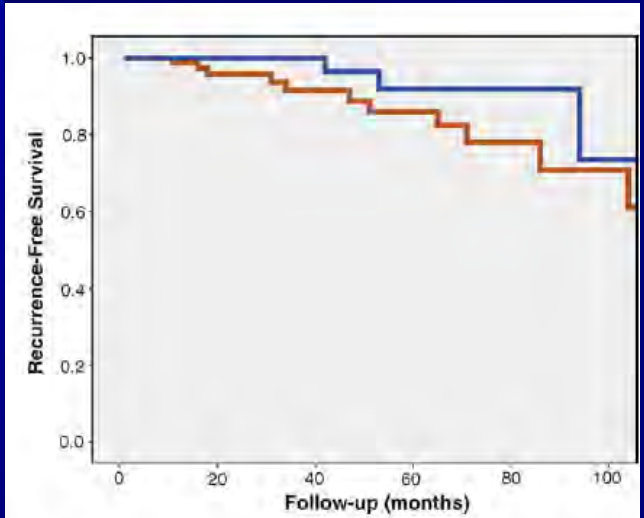


Fig. 1 – Recurrence-free survival according to margin status. There is no difference between negative (blue) and positive (orange) margin patients, which is significant (log-rank test, $p = 0.113$).

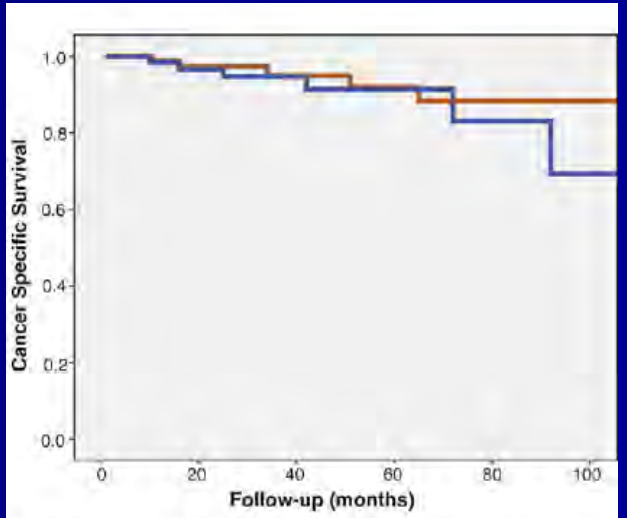


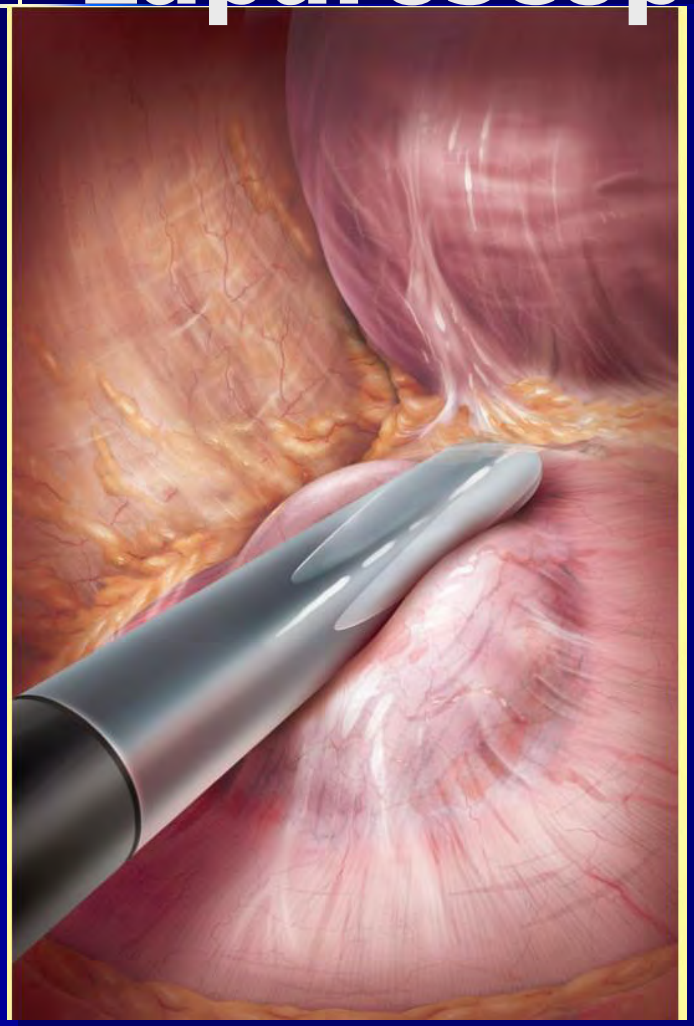
Fig. 2 – Cancer-specific survival curves according to margin status. Survival of negative (blue) and positive (orange) margin patients is similar (log-rank test, $p = 0.42$).

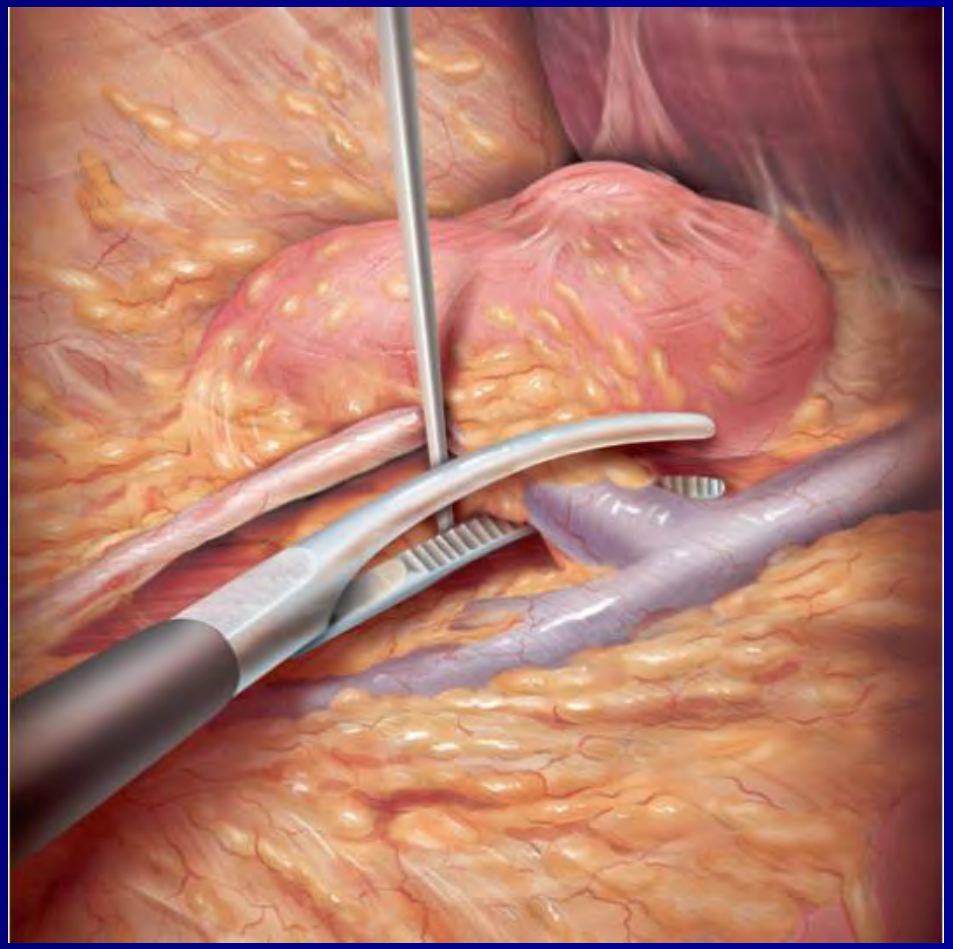
sopravvivenza libera da malattia

sopravvivenza cancro-specifica

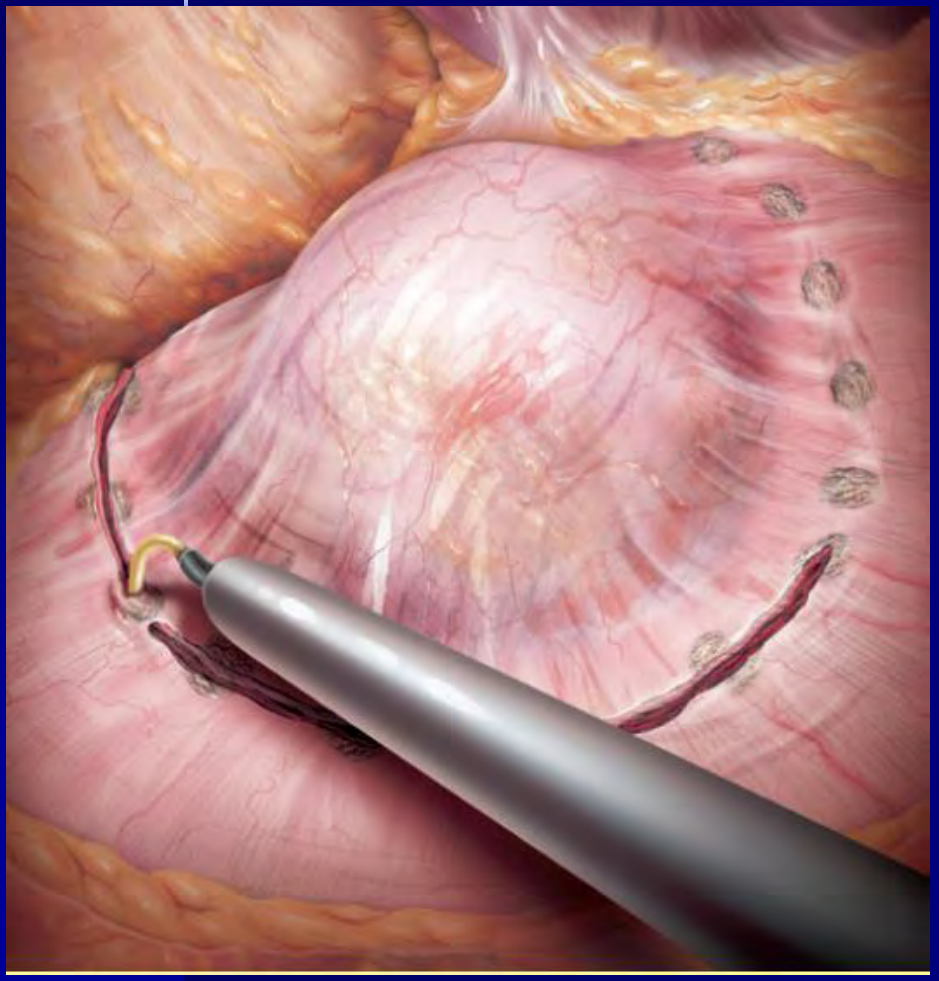
EUROPEAN UROLOGY 57 (2010) 466–473

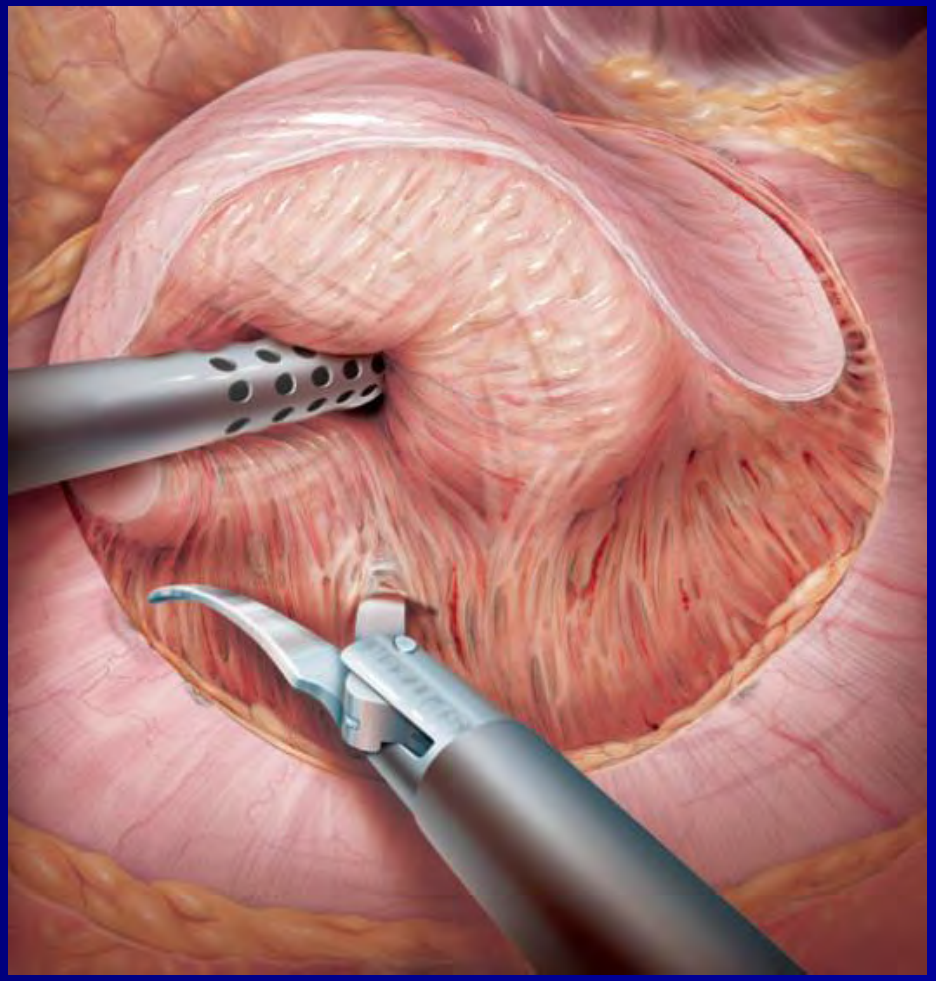
Enucleoresezione Dettagli di Tecnica Laparoscopica



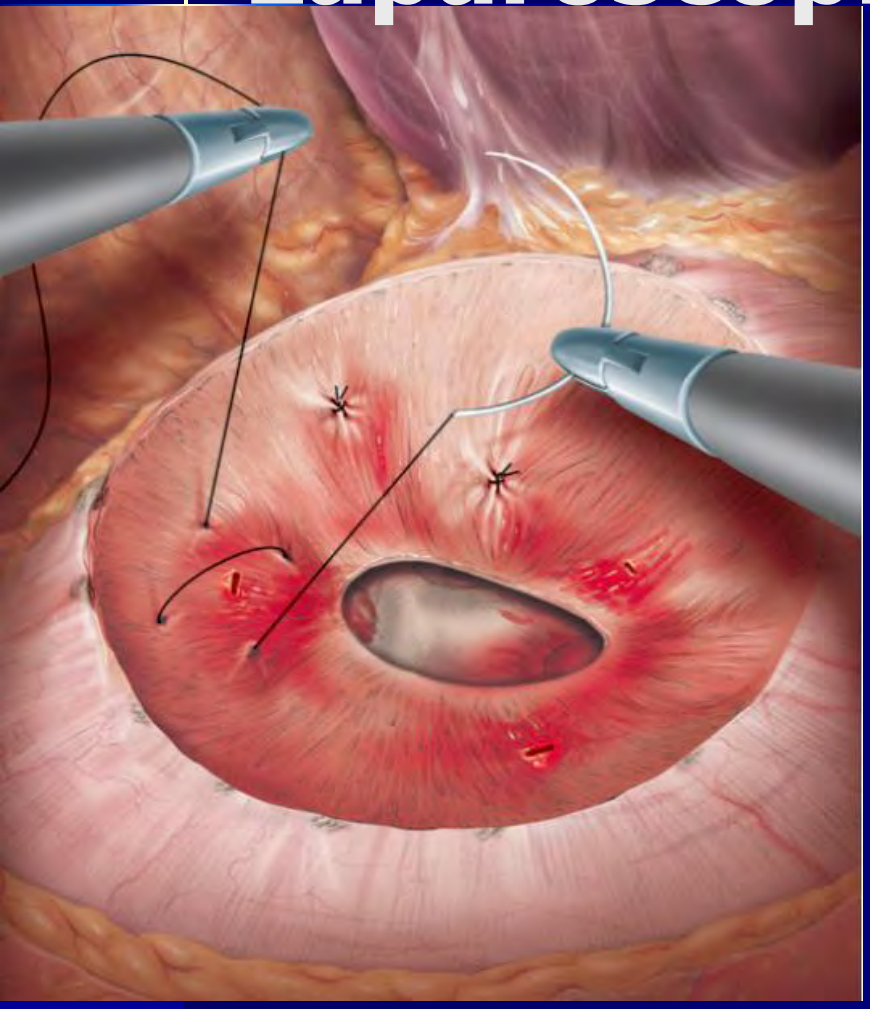


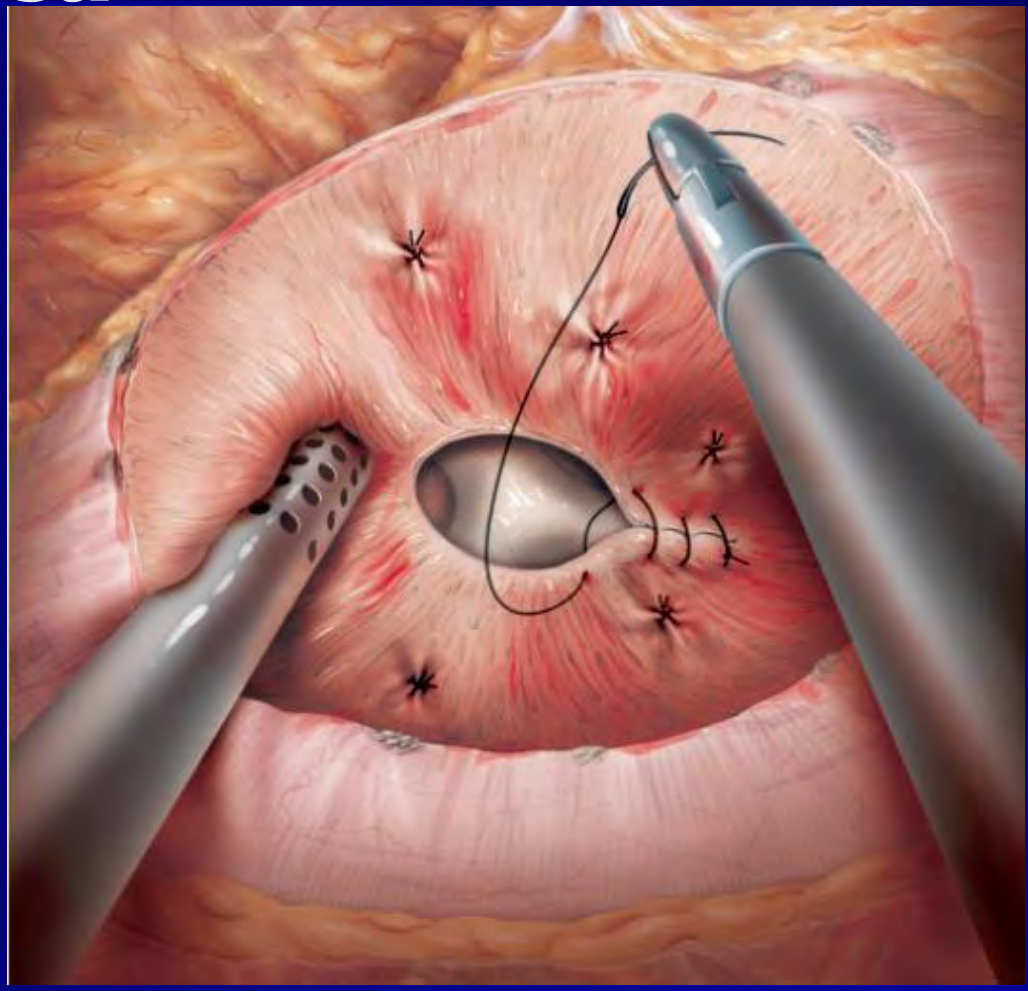
Enucleoresezione Dettagli di Tecnica Laparoscopica



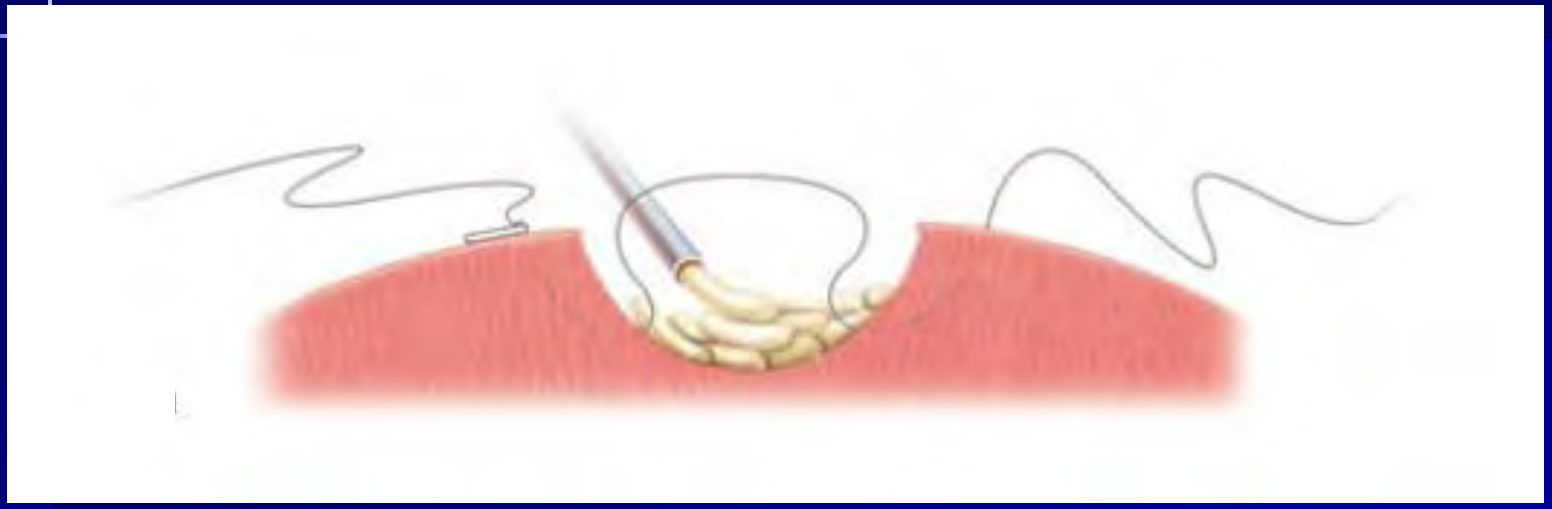


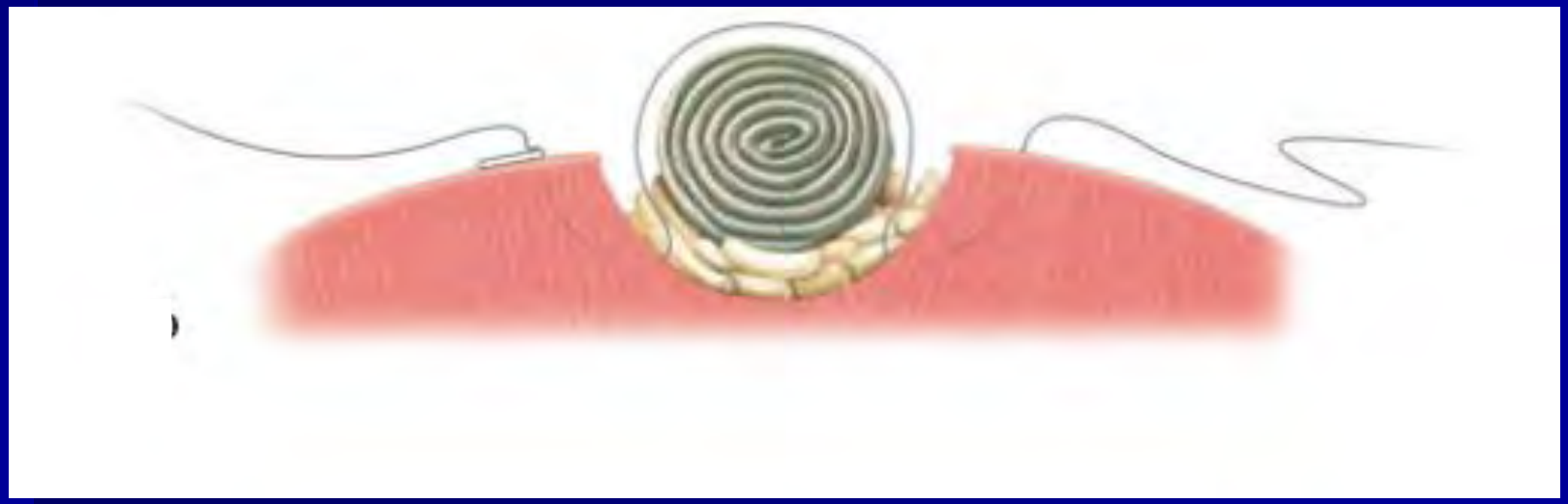
Enucleoresezione Dettagli di Tecnica Laparoscopica



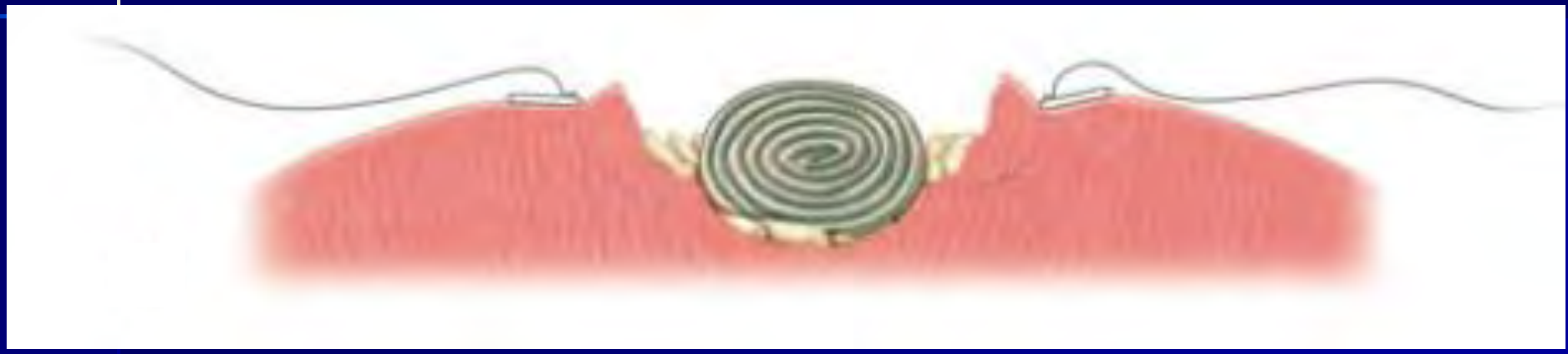


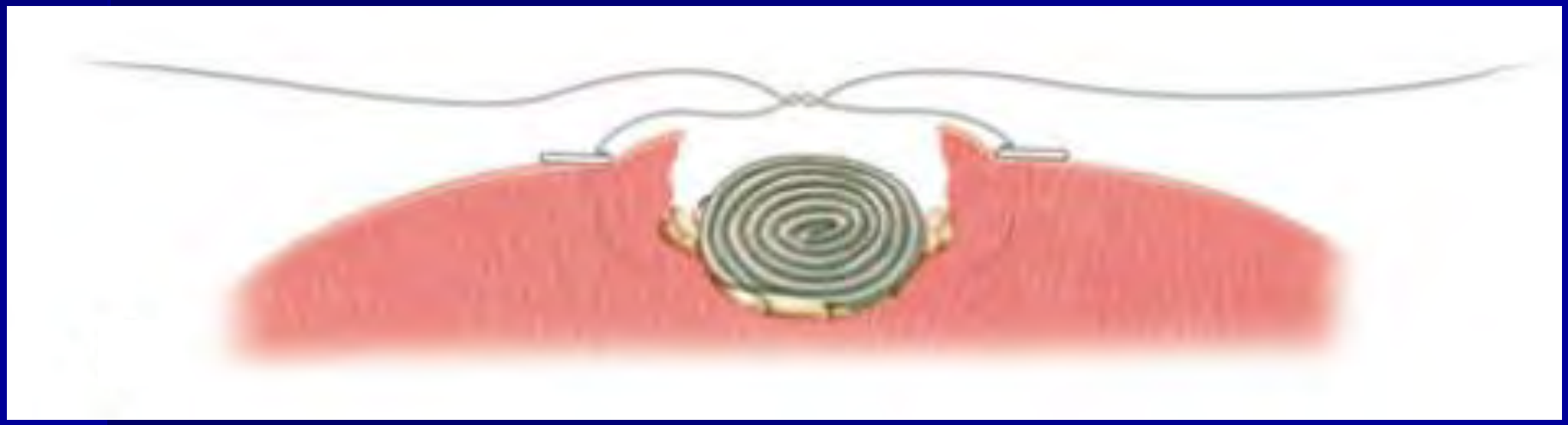
Enucleoresezione
Dettagli di Tecnica: Controllo Emostasi



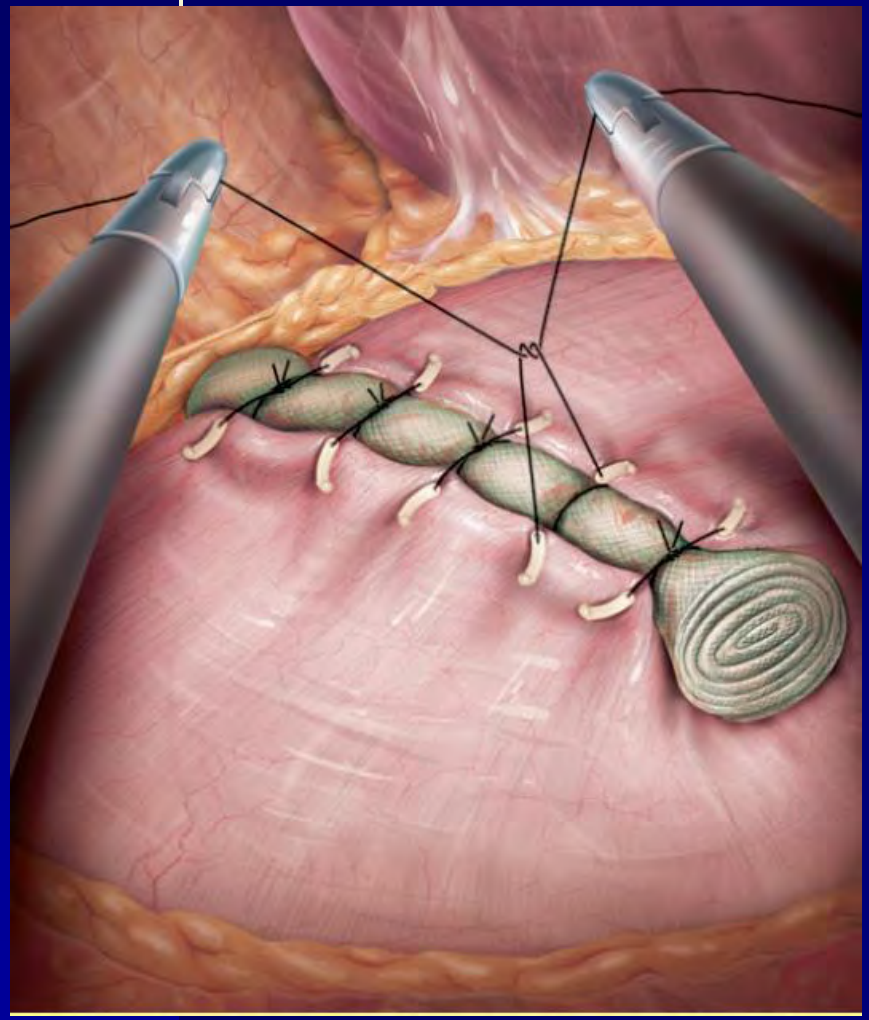


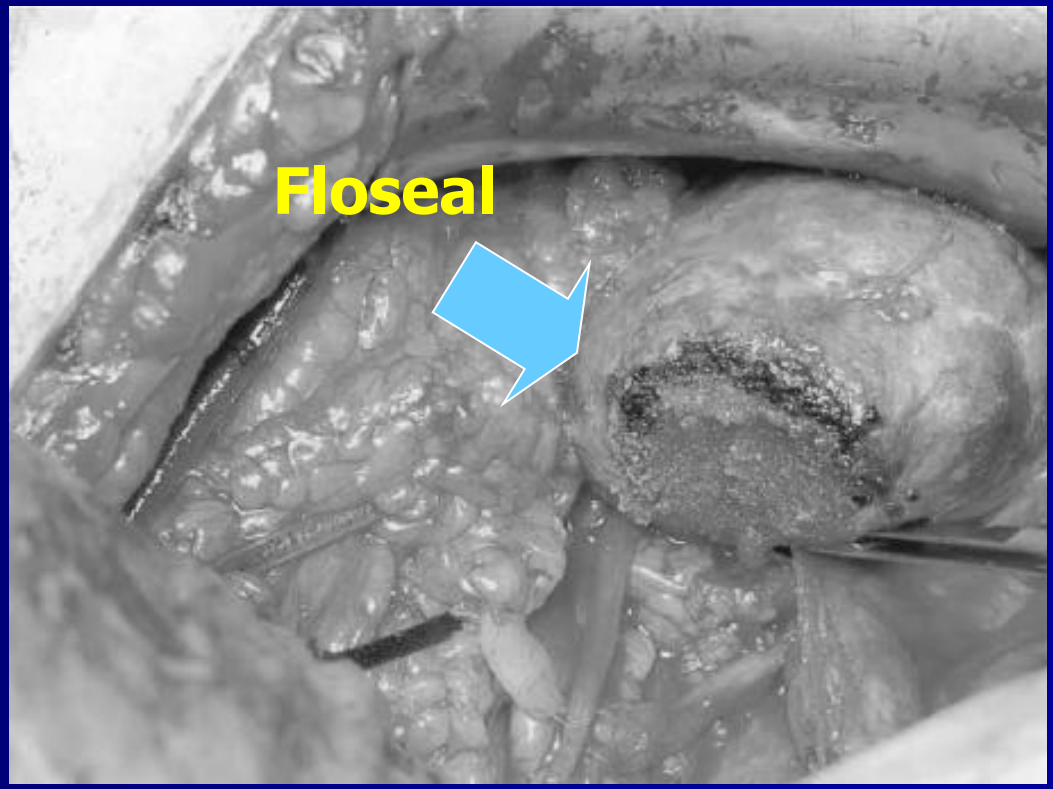
Enucleoresezione
Dettagli di Tecnica: Controllo Emostasi





Enucleoresezione
Dettagli di Tecnica: Controllo Emostasi





Risultati Laparoscopic NSS

Follow-up	pts	Tumore (cm)	Recidiva locale (%)	Complicanze *	Cancer Survival %
3 Anni	**477**	**2 - 3**	**1,4 - 4,2**	**4 - 16 %**	**100**

*** Sanguinamenti 1,3-8%; Fistole urinarie 2-8%**

Lane BR and Novick AC, BJU 2007
Aron M and Gill IS, BJU 2007

Risultati
Open vs Laparoscopic NSS

Follow-up	pts	Tumore > 4 cm	Tempo Ischemia	Perdite ematiche	Complicanze	Degenza	Ripresa
Open*	**595**	**39%**	**20 min**	**364**	**15,3 %**	**6,1**	**12 sett**
Lap	**454**	**8,4%**	**31 min**	**262**	**20 %**	**3,1**	**4 sett**

*** Pazienti 7,3% con ridotta funzionalità renale e 31% pts monorene**

Sopravvivenza cancro specifica > 99% a 3 anni in entrambi gruppi

Lane BR and Novick AC, BJU 2007

Risultati
Open vs Laparoscopic NSS

- 1,800 pts RCC ≤ 7 cm
- Funzionalità renale e sopravvivenza libera da malattia sovrapponibile a 3 anni per LPN vs OPN

Factors associated with LPN	*P*-value
Shorter operative time	< 0.0001
Reduced operative blood loss	< 0.0001
Shorter hospital stay	< 0.0001
Longer ischemia time	< 0.0001
Postoperative urologic complications	< 0.0001
Increased N of subsequent procedures	< 0.0001

LP è associata a maggiore morbilità post-operatoria

Gill IS, ABS 495, AUA 2007

Risultati
Open vs Laparoscopic NSS

- 221 pts RCC ≤ 7 cm in rene unico

	OPN (N=189)	LPN (N=32)
Median tumour size (cm)	3.9	2.8
Median warm ischemia (min)	21	30.5
Transfusion (% of pts)	8	6
Postoperative complications (% of pts)	24	45
Urologic complications (% of pts)	10	15
Chronic renal failure (% of pts)	2	9

LP NSS è associata a maggiore morbilità e tempi di ischemia più lunghi

Lane BR, ABS 648, AUA 2007

Collaborative Review – Kidney Cancer

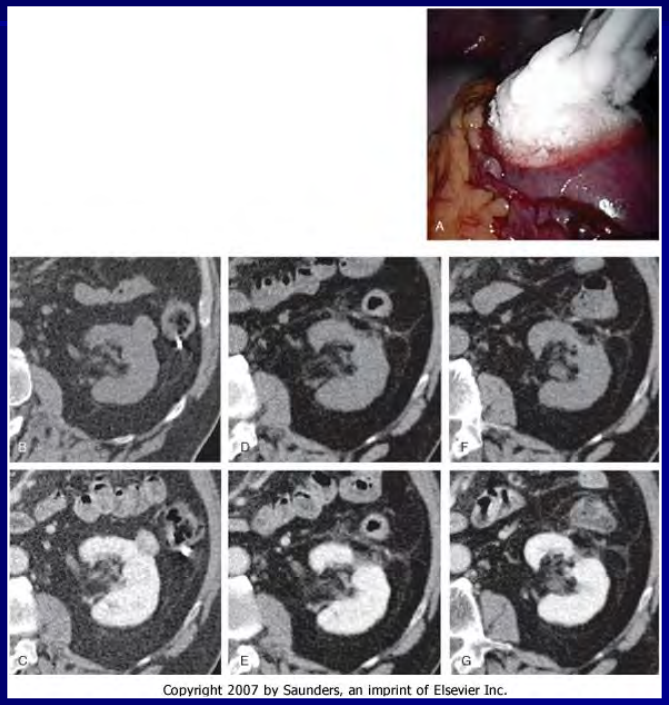
The Expanding Role of Partial Nephrectomy: A Critical Analysis of Indications, Results, and Complications

Karim Touijer[a,*], *Didier Jacqmin*[b], *Louis R. Kavoussi*[c], *Francesco Montorsi*[d], *Jean Jacques Patard*[e], *Craig G. Rogers*[f], *Paul Russo*[a], *Robert G. Uzzo*[g], *Hendrik Van Poppel*[h]

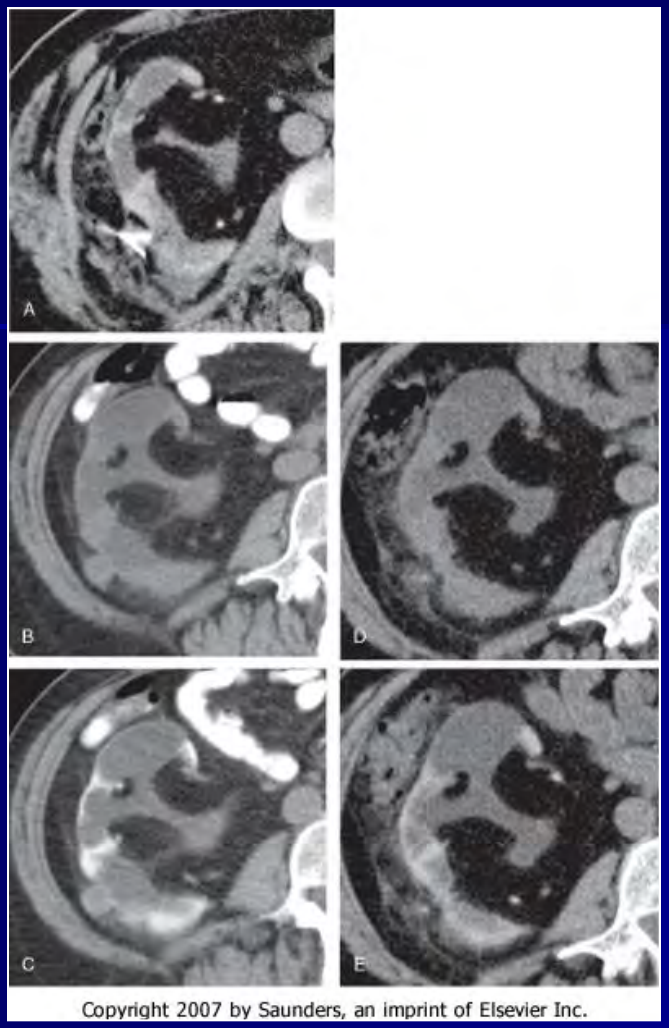
"...Therefore, given the negative impact of RN (as shown above), PN seems defendable when technically feasible and is oncologically safe even for larger tumours".

EUROPEAN UROLOGY 57 (2010) 214–222

TECNICHE DI ABLAZIONE:CRIOABLAZIONE E ABLAZIONE CON RADIOFREQUENZE



Biopsy-proved clear cell renal cell cancer 2.5 cm in diameter: intraoperative image during laparoscopic cryoablation with evolving ice ball (A), unenhanced and contrast-enhanced computed tomography scans preoperatively (B and C), after 3 months (D and E), and after 9 months (F and G) showing complete loss of enhancement and progressive shrinking of lesion.



Percutaneous radiofrequency (RF) ablation of biopsy-proved papillary cancer in a hydronephrotic kidney after multiple stone episodes: monopolar RF probe in tumor (A) and unenhanced and contrast-enhanced computed tomography scans before (B and C) and 6 months (D and E) after RF ablation showing complete loss of contrast enhancement and fibrotic shrinking of lesion.

- Radiofrequency and cryoablation are the only minimally invasive approaches for the treatment of small renal tumours with medium follow-up data.

- Although the oncological efficacy is not yet known, currently available data strongly suggest that cryoablation, when performed laparoscopically, results in fewer re-treatments and improved local tumour control compared with RFA (level of evidence: 3).

- For both RFA and cryoablation, recurrence rates are higher than with nephron-sparing surgery (83-86) (level of evidence: 3).

(EAU Guidelines 2010)

OSSERVAZIONI: accesso *open*

- ampia esposizione del campo operatorio
- facilità e rapidità di manovra
- tempi di ischemia a caldo attualmente più brevi rispetto alla laparoscopia (14-20 min vs 27-35 min)
- possibilità di ischemia a freddo

OSSERVAZIONI: accesso *open*

- più agevole risoluzione di eventuali complicanze emorragiche
- accurata ricostruzione della via escretrice e del parenchima renale

OSSERVAZIONI: accesso *laparoscopico*

- Tempi operatori ridotti (..in mani esperte)
- Ridotte perdite ematiche
- Minore durata della degenza ospedaliera
- Rapido ritorno alle attività quotidiane

CONCLUSIONI

- nel trattamento del RCC, la NSS si è dimostrata metodica affidabile e oncologicamente valida
- elevato rischio di IRC dopo nefrectomia radicale
- gli ottimi risultati nel trattamento di RCC fino a 7 cm, ampliano i limiti della NSS, soprattutto open

- nonostante gli ottimi risultati, la NSS risulta essere ancora sottoutilizzata
- si è registrato finora un ampio ricorso a favore della "miniinvasiva" nefrectomia radicale laparoscopica

…La miniinvasività vale il sacrificio di un rene intero?

"nephron-sparing surgery is a safe procedure from the oncological point of view. Whenever technically feasible, nephron-sparing surgery is therefore considered to be the standard of care for T1a/b stage RCC " (EAU Guidelines 2010)