

# PATOLOG GÖZÜYLE BÖBREK TÜMÖRLERİ

Prof. Dr. Kutsal YÖRÜKOĞLU  
Dokuz Eylül Üniversitesi Tıp Fakültesi  
Patoloji Anabilim Dalı

ANTAKYA 2008



# SINIFLAMA (WHO 2004)



- Renal hücreli tümörler

Konvansiyonel (berrak hücreli) RHK

Multiloküler kistik RHK

Papiller (kromofil) RHK

Kromofob RHK

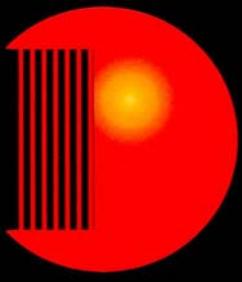
Toplayıcı duktus (Bellini) karsinomu

Renal medüller karsinom

Xp11 translokasyon karsinomları

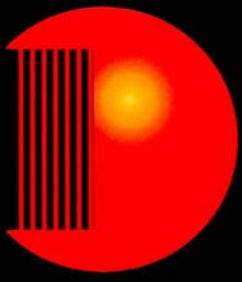
Müsinöz tubuler ve iğsi hücreli karsinom

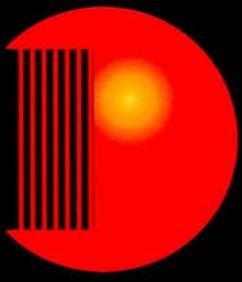
RHK, sınıflandırılmayan



# SINIFLAMA

- **Benign**
  - Papiller adenom
  - Onkositom
- **Metanefrik tümörler**
  - Metanefrik adenom
  - Metanefrik adenofibrom
  - Metanefrik stromal tümör
- **Nöroblastik tümörler**
- **Mezenkimal tümörler**
- **Mikst mezenkimal-epitelyal tümörler**
  - Mikst epitelyal stromal tümör
- **Nöroendokrin tümörler**
- **Lenfoid tümörler**
- **Germ hücreli tümörler**
- **Metastatik tümörler**

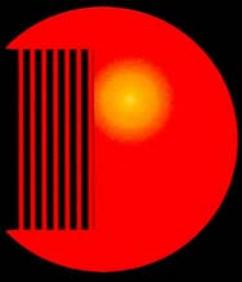




# PROGNOSTİK FAKTÖRLER

1. Anlamlı olması,
2. Bağımsız olması,
3. Klinik önemli ve tedaviyi yönlendirebilir olması gerekir. . . .

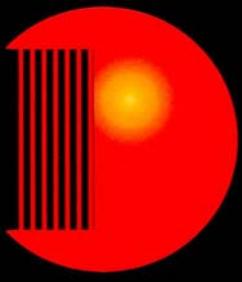
American Joint Committee on Cancer



# PROGNOSTİK FAKTÖRLER

1. Anlamalı olması,
2. Bağımsız olması,
3. Klinik önemli ve tedaviyi yönlendirebilir,
4. Tekrarlanabilir, ucuz, klinik uyumu sağlanmış ve uygulanabilir olması gerekir. . . .

National Institute of Health



# PROGNOSTİK FAKTÖRLER

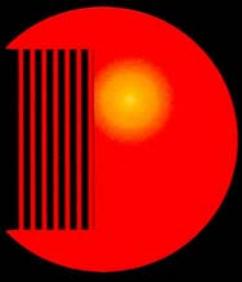
1. Literatürle iyi desteklenmiş ve/veya tedavide kullanılabilir,
2. a. Biyolojik veya b. Klinik geniş serilerde çalışılmış,
3. Diğerleri. . .

College of American Pathologists



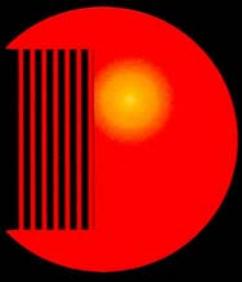
# CAP I

- Hasta ile ilişkili
  - Semptomatik tümör
  - Düşük performans. . .
- Tümör ile ilişkili
  - Evre
  - Derece
  - Histolojik tür
  - Sarkomatoid yapı
  - Cerrahi sınır
  - Metastaz (sayısı, rezektabilite, lokalizasyon)



## CAP II

- Toplayıcı duktus karsinomu
- Nükleer morfometri
- Anöploidi
- Ki-67 indeksi
- AgNOR



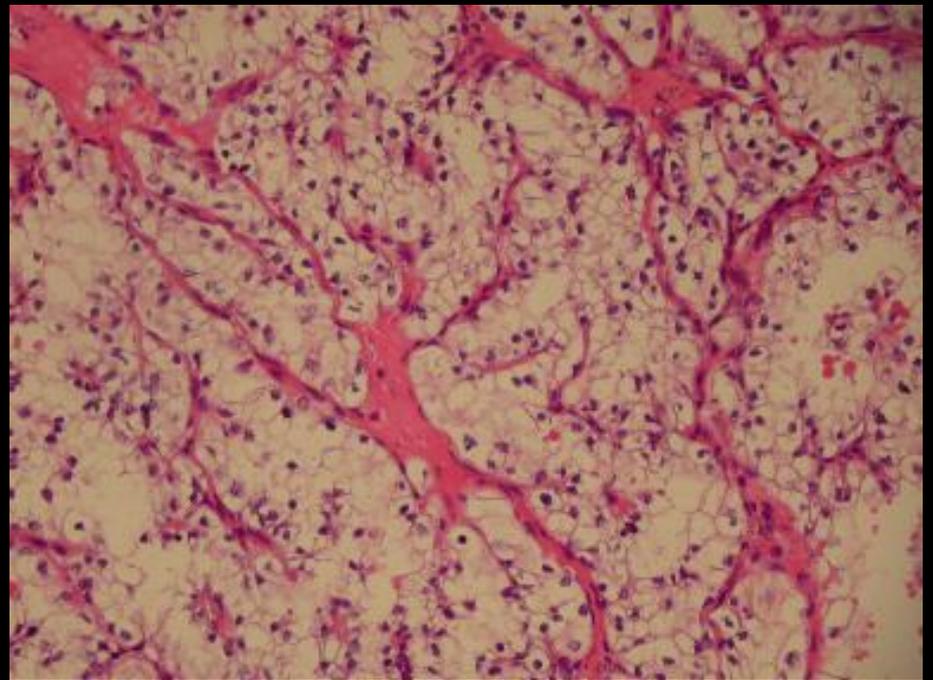
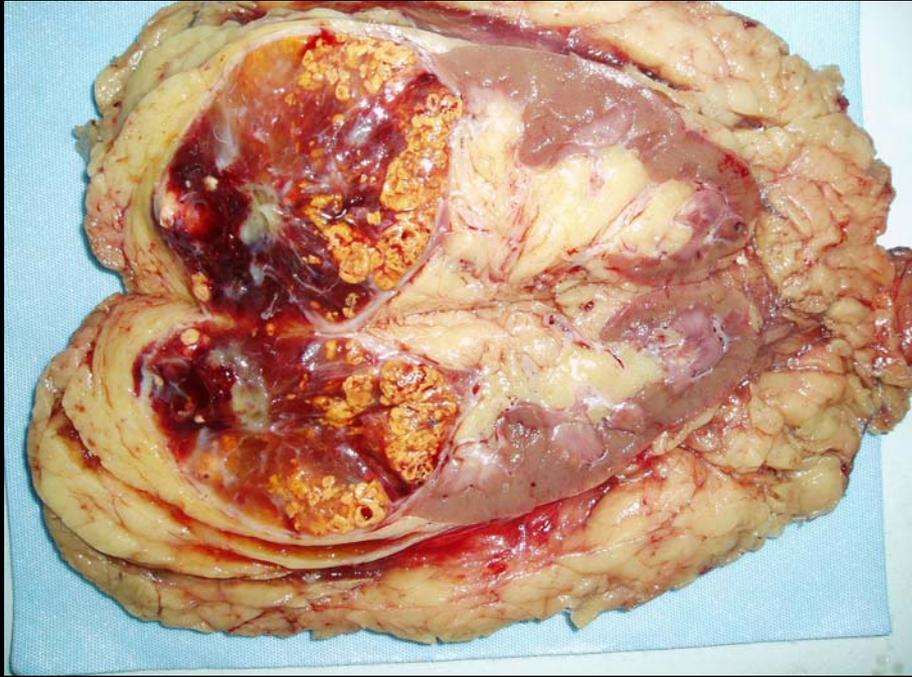
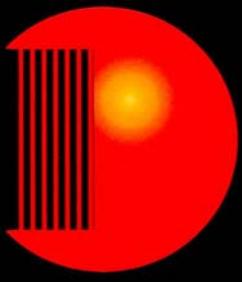
# CAP III

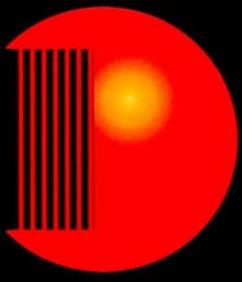
- p53
- bcl-2
- Büyüme faktörleri
- Adezyon molekülleri
- Anjiogenez
- Sitokinler
- Sitogenetik
- Diğerleri





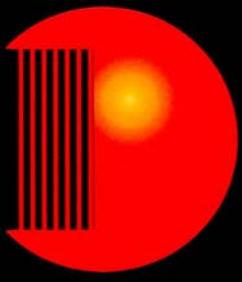
# KONVANSİYONEL RHK





# KONVANSİYONEL RHK

- Granüler sitoplazmalı
  - Konvansiyonel RHK
  - Kromofob RHK
  - Papiller RHK
  - Onkositom
  - Epiteloid anjiyomyolipom
- 3p delesyonu
  - ~~Berrak hücreli adenom~~
- VHL gen mutasyonu
  - VHL hastalığı
  - Sporadik



# KONVANSİYONEL RHK

-3p (FISH, LOH, CGH)

çoğunda, ilk

VHL mut (%34-56)

DNA metilasyonu

-9p, -14q (kötü prognostik)

VHL proteini

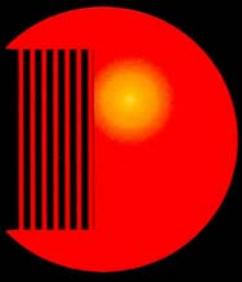


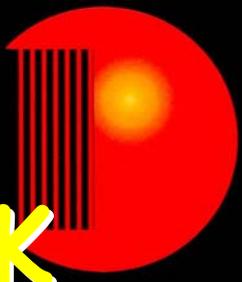
hipoksiyle uyarılabilen faktör

hücre prolifer.

neovaskülarizasyon

ekstrasel. matriks oluşumu





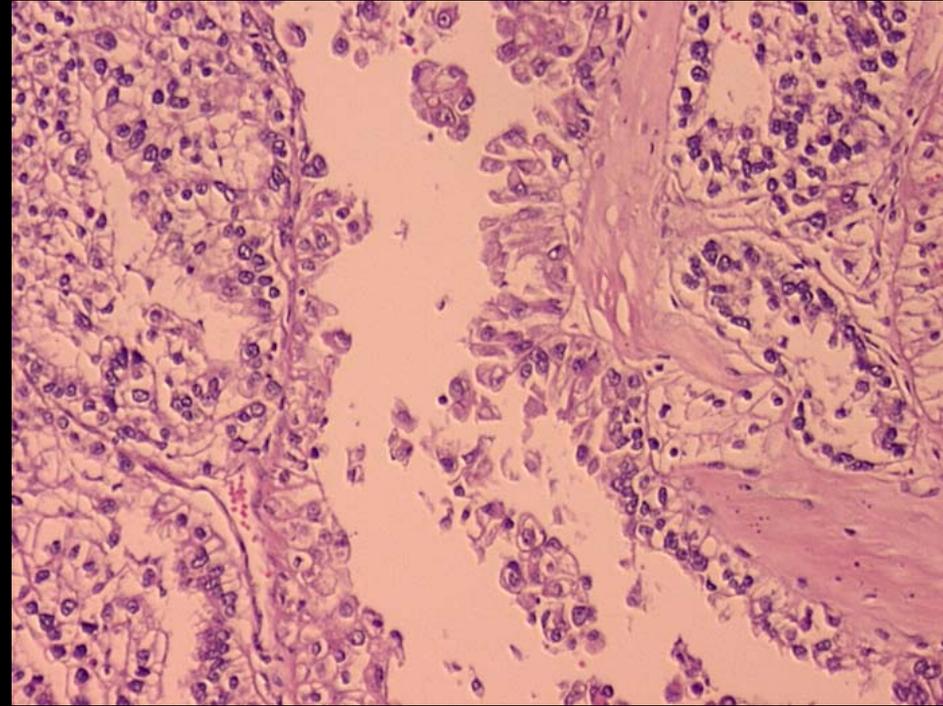
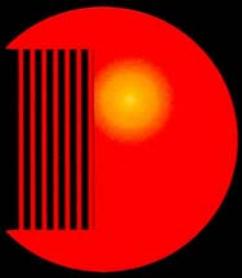
# MULTILOKÜLER KİSTİK RHK

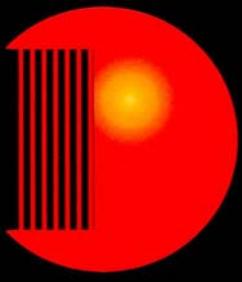






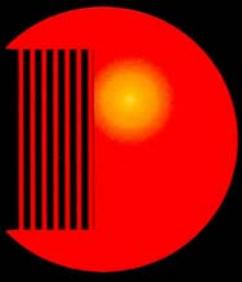
# XP11 TRANSLOKASYONLU RHK





# AİLESEL RHK

- VHL
  - Konvansiyonel RHK
- Herediter papiller RHK
  - Tip I papiller RHK
  - C-met (tirozin kinaz)
- Herediter leiomyom RHK
  - Tip II Papiller RHK
  - Fumarat hidrataz
- Birt-Hogg-Dube sendromu
  - Kromofob RHK ve onkositom
  - BHD geni (17. kromozom)

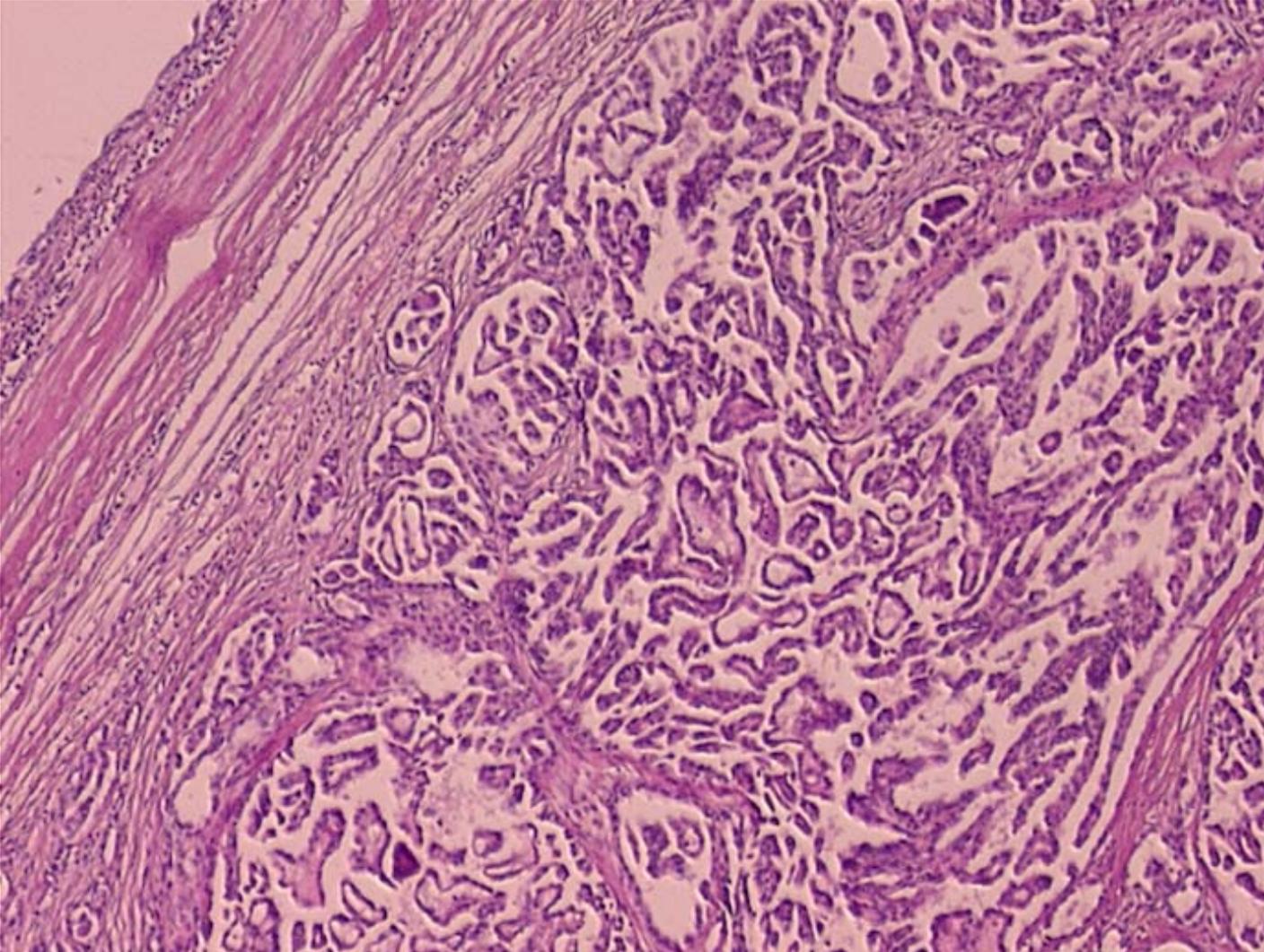
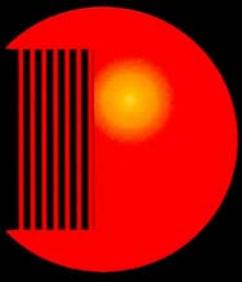


# PAPİLLER RHK



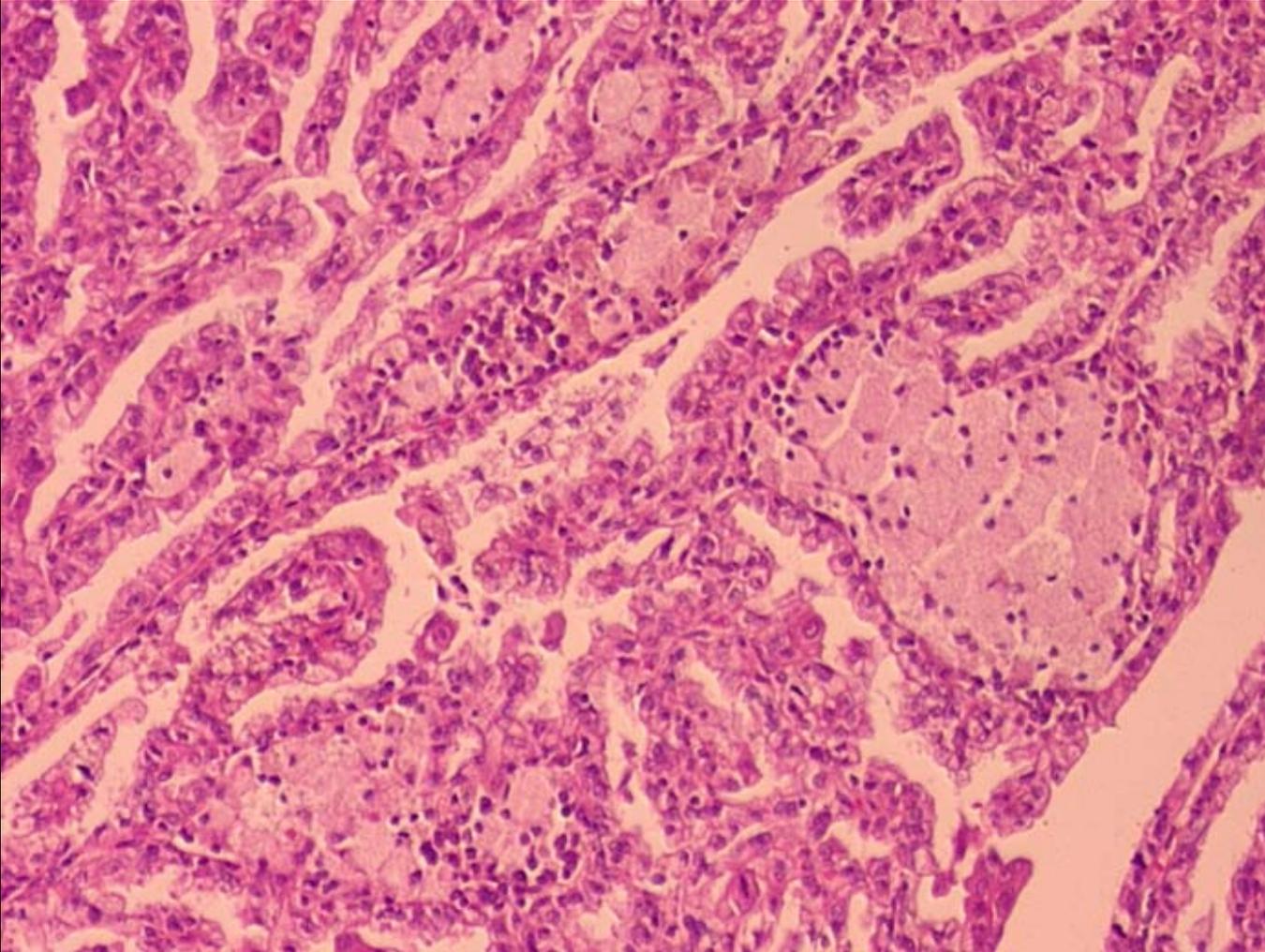
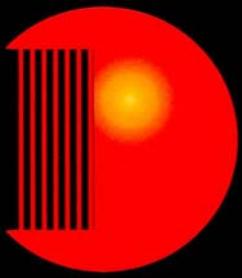


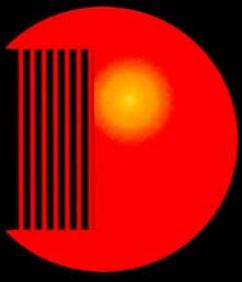
# TIP I PAPİLLER RHK





# TIP II PAPİLLER RHK





# PAPİLLER RHK

+7, +17

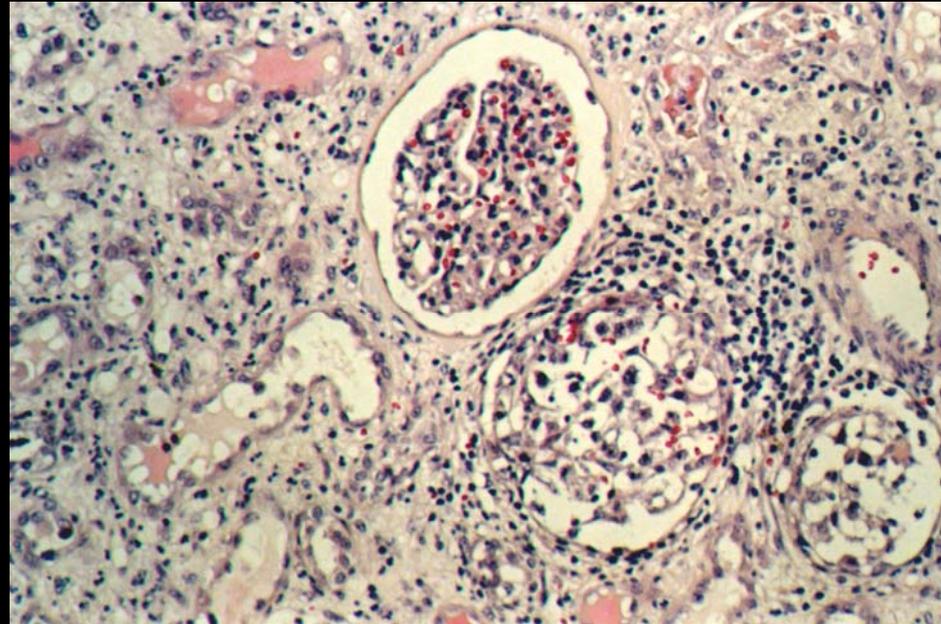
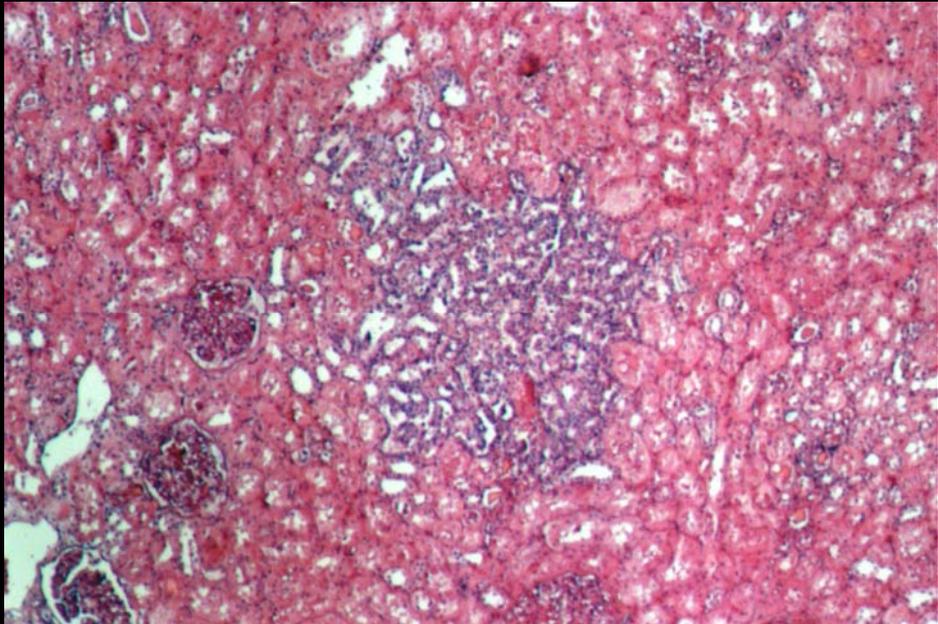
-y

+12, +16, +20 (progresyon)

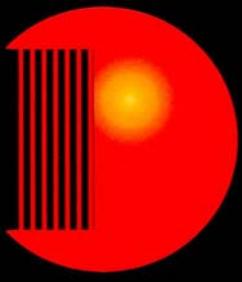
- Tip I: İyi prognozlu
- Tip II: ileri evre, derece ve progresyon ile ilişkili
- Nekroz iyi prognostik gösterge

# ADENOM $\alpha$ RHK

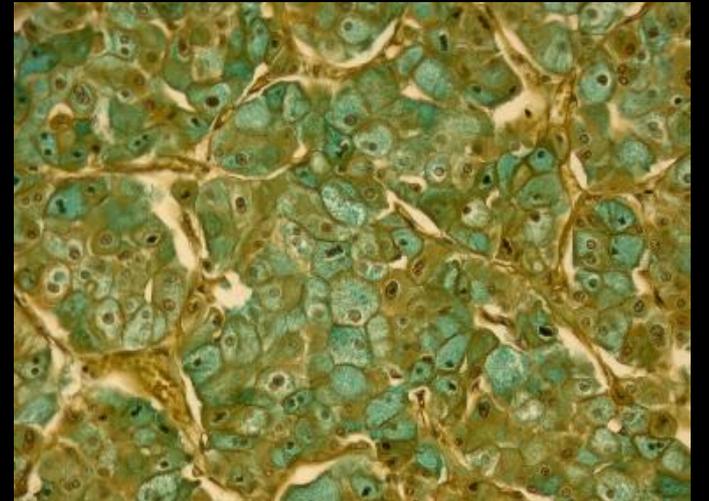
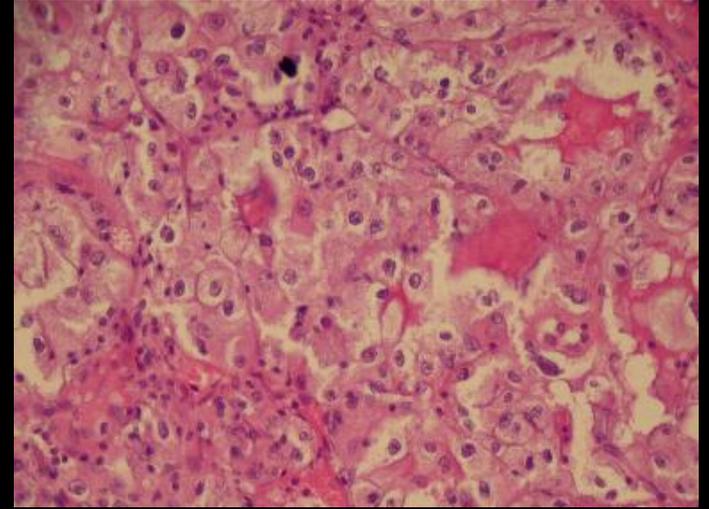
- Papiller adenom - 5 mm
- Berrak hücre

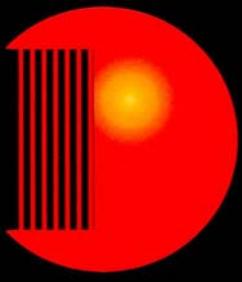






# KROMOFOB RHK





# KROMOFOB RHK

-1,-2,-6,-10,-13,-17,-21

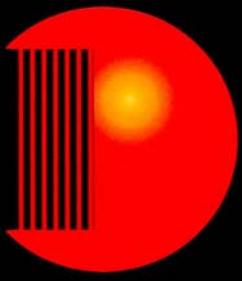
PTEN LOH

hipodiploid DNA

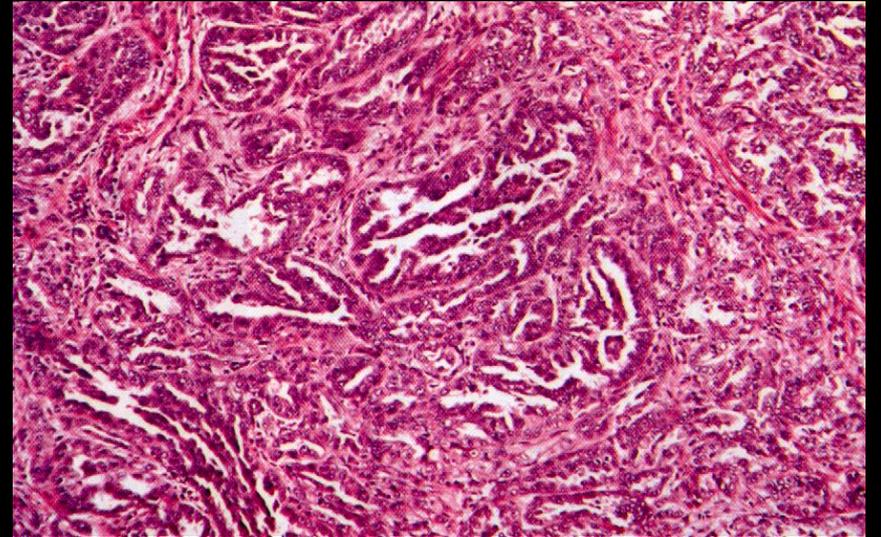
- En iyi prognozlu tür
- Sarkomatoid gelişim !
  - İnterleukin-2 cevabı kötü (papiller RHK)

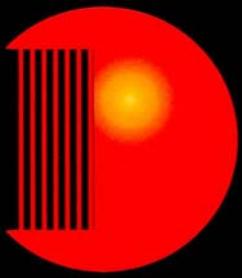


# TOPLAYICI DUKTUS KARSİNOMU



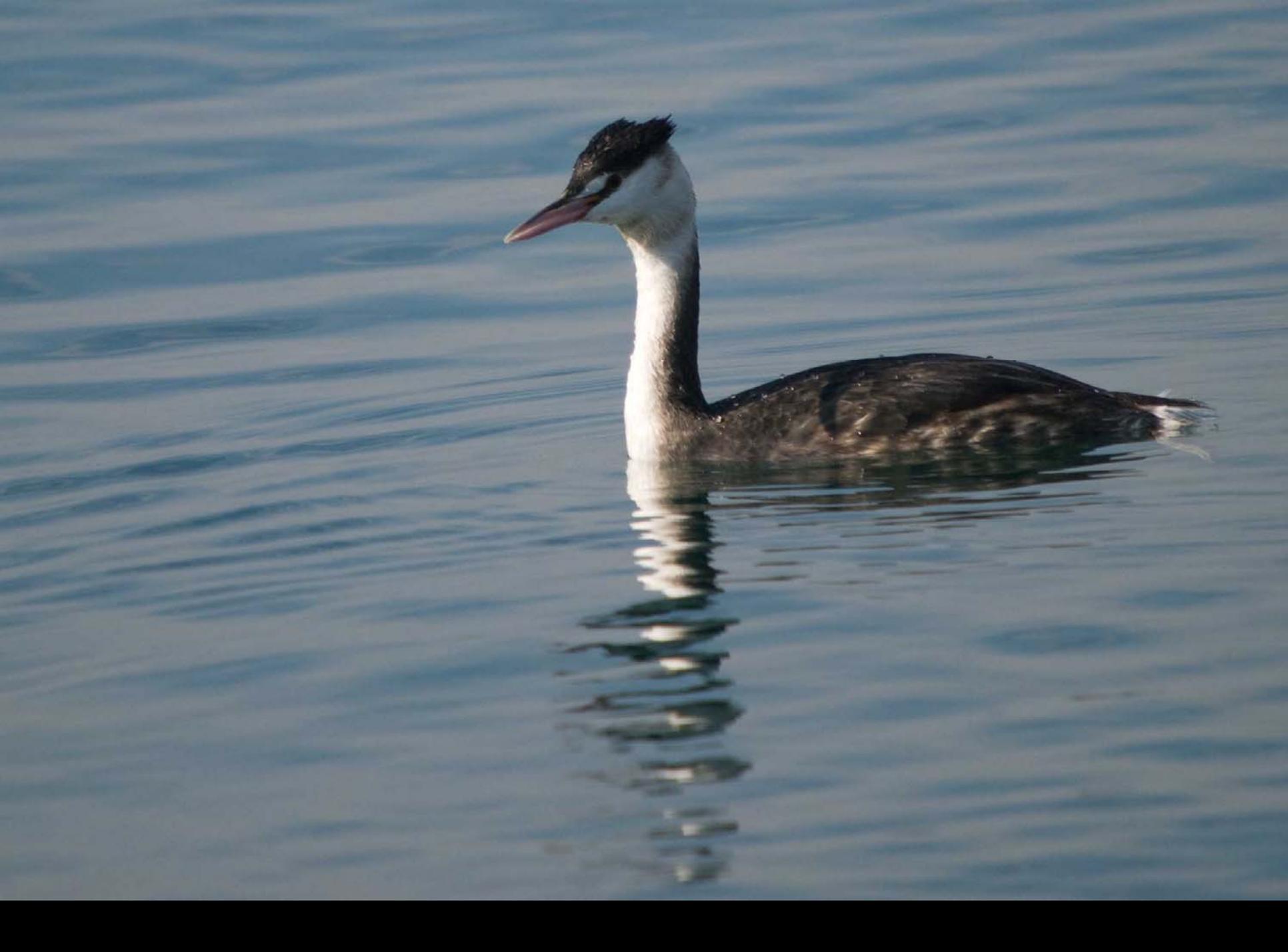
- Yerleşim
- Prognoz
- Tanı

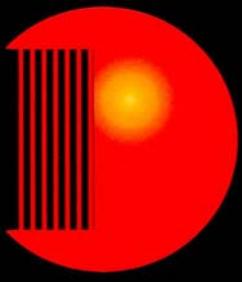




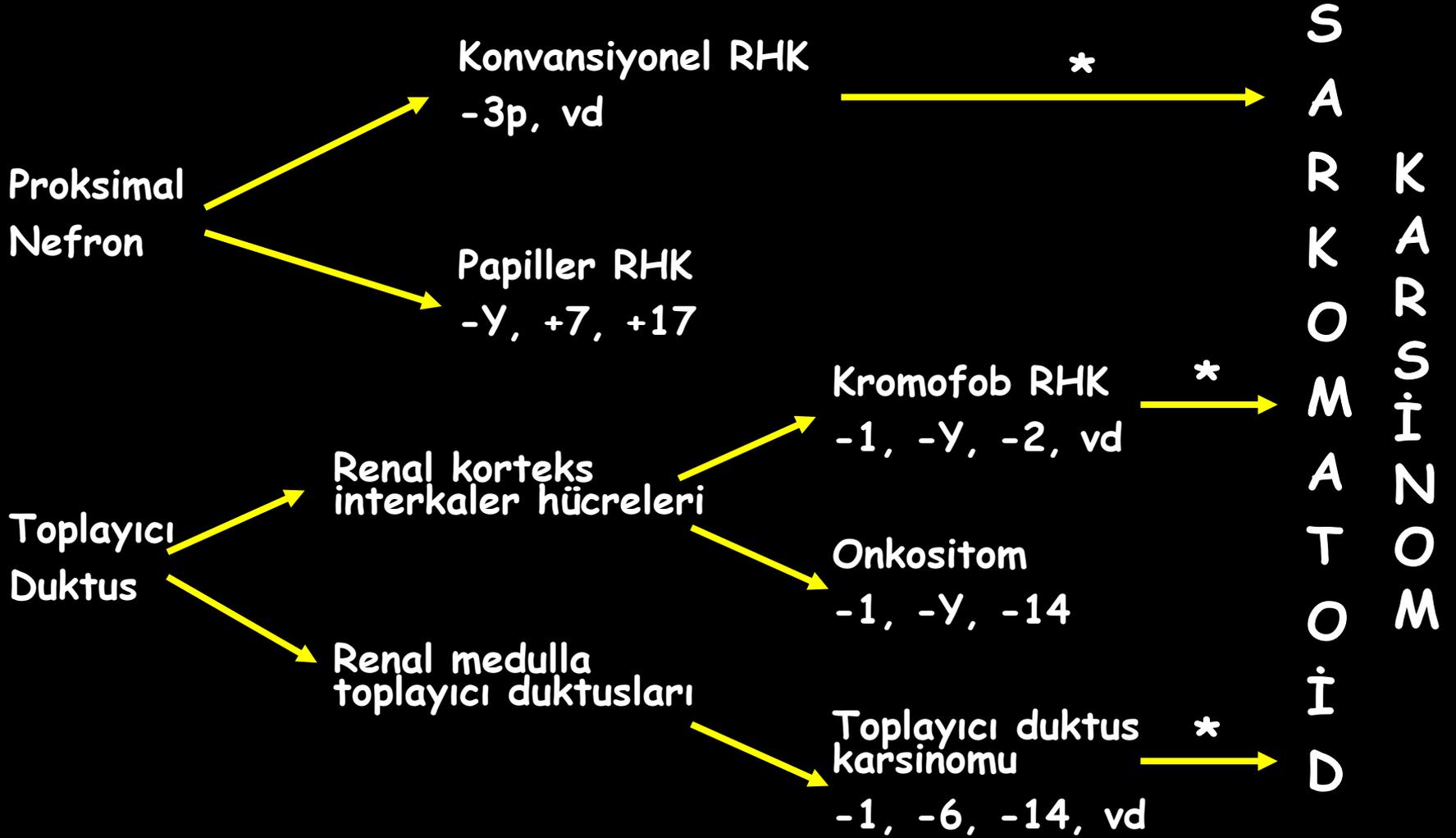
# TOPLAYICI DUKTUS KARSİNOMU

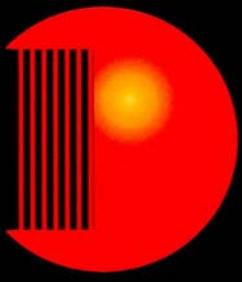
- -18, -21, -Y
- 1q, 6p, 13q, 21q LOH
- -3p



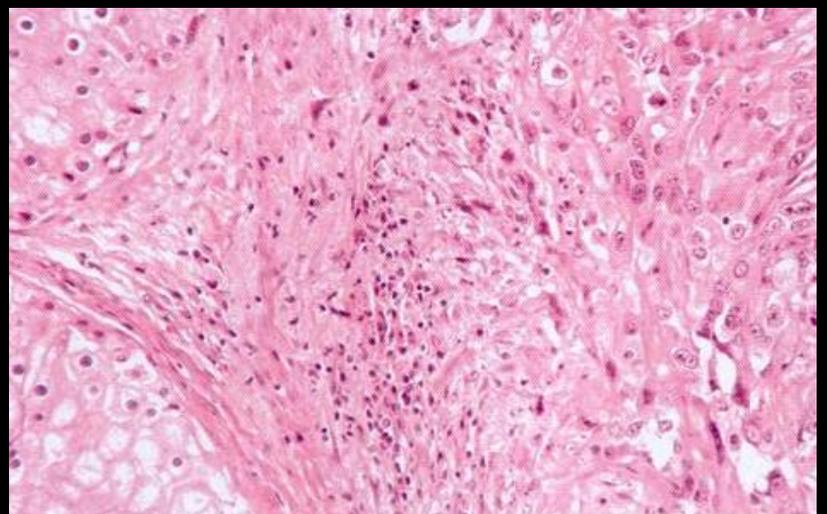
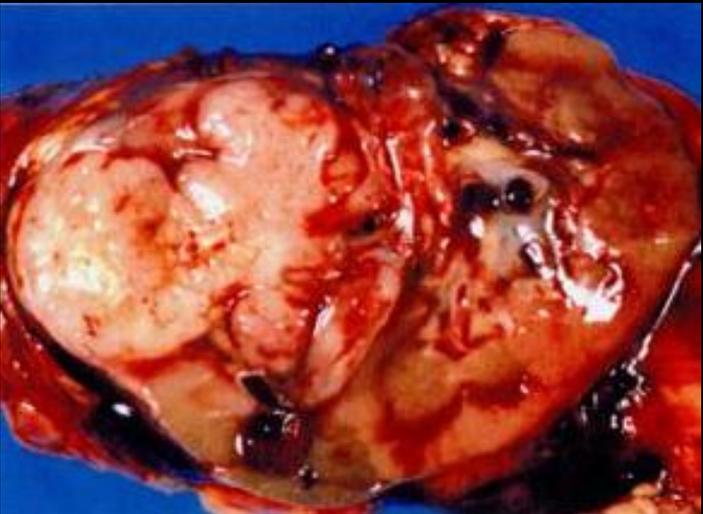
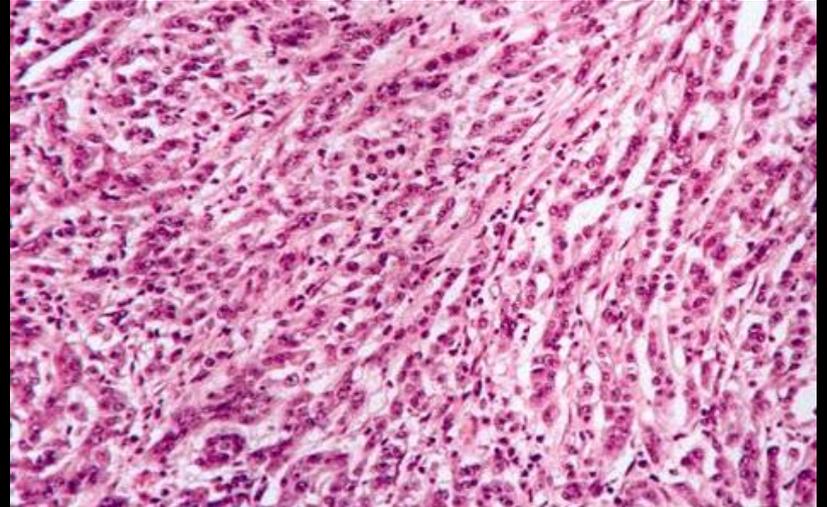
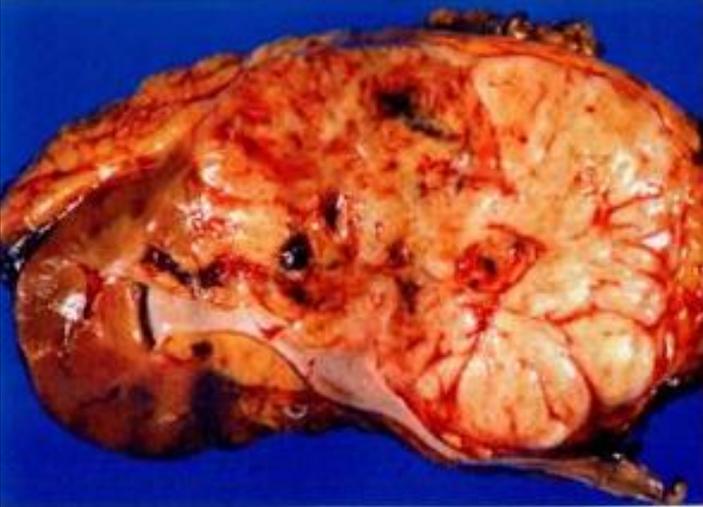


# SARKOMATOİD RHK

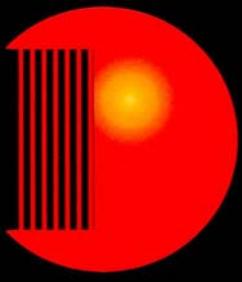




# SARKOMATOİD RHK





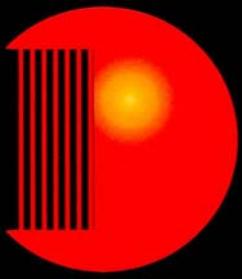


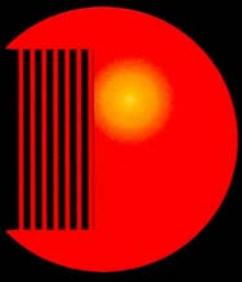
# RENAL MEDÜLLER KARSİNOM

- 20-40 YAŞ
- Orak hücreli anemi
- 37 olgu
- -11
- Agresif



# MÜSİNÖZ TUBULER İĞSİ HÜCRELİ KARSİNOM



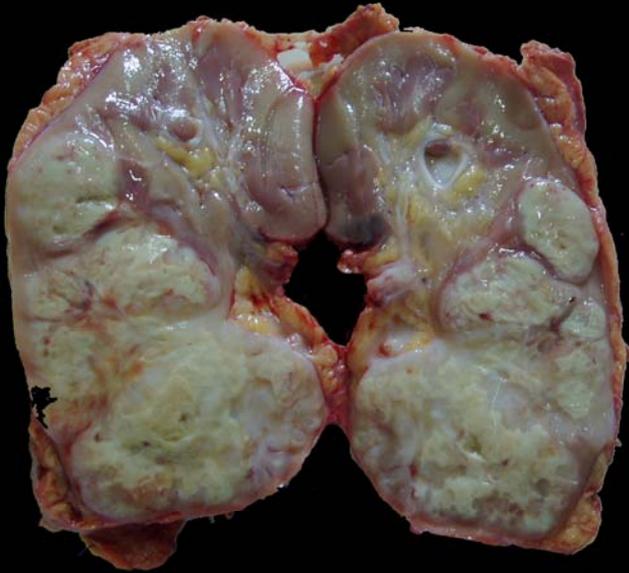
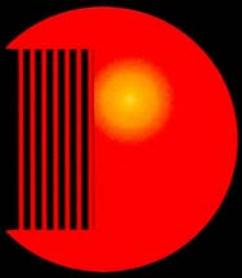


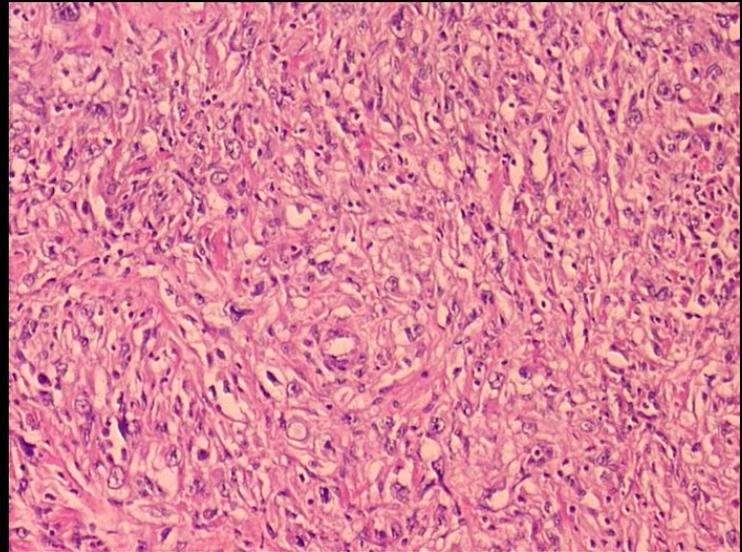
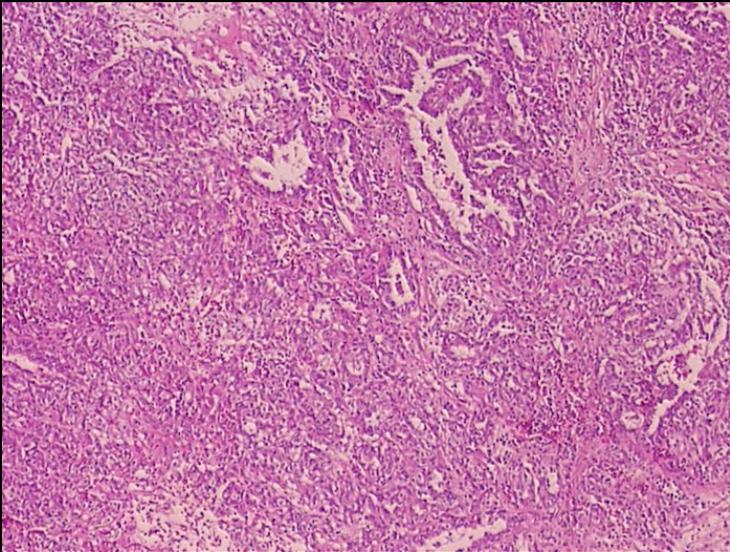
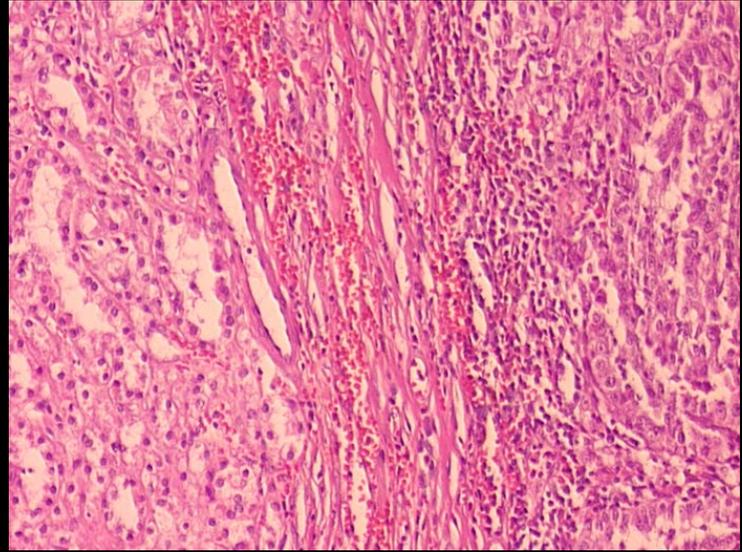
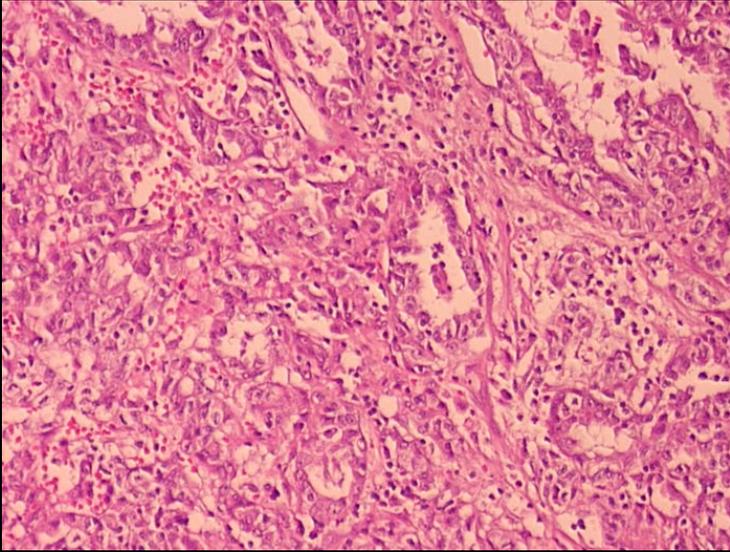
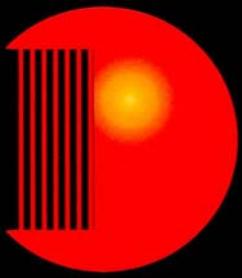
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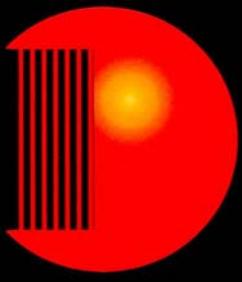
- 17-82 YAŞ
- E/K : 1/4
- -1, -4, -6, -8, -13, -14
- +7, +11, +16, +17
- İyi prognozlu



# SINIFLANDIRILAMAYAN RHK



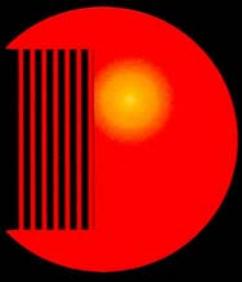






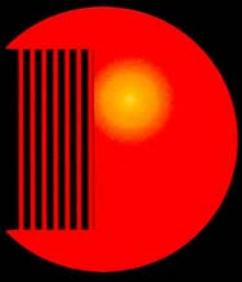
	Berrak	Papiller	Kromofob	Sınıfl.
<b>Sıklık</b>	<b>63</b>	<b>18 (5/10)</b>	<b>6</b>	<b>6</b>
<b>Yaş</b>	<b>61</b>	<b>58</b>	<b>59</b>	<b>61</b>
<b>E/K</b>	<b>1.6/1</b>	<b>1.6/1</b>	<b>1.4/1</b>	<b>1.8/1</b>
<b>Multifokalite</b>	<b>6,7</b>	<b>22.5</b>	<b>83</b>	
<b>Semptomatik</b>	<b>59</b>	<b>52</b>	<b>42</b>	<b>39</b>
<b>pT1-pT2</b>	<b>63</b>	<b>79</b>	<b>88</b>	<b>7</b>
<b>Sarkomatoid</b>	<b>8</b>	<b>4</b>	<b>10</b>	<b>11</b>
<b>Hastalığa bağlı ölüm</b>	<b>24</b>	<b>14</b>	<b>5</b>	<b>65</b>
<b>Hastalığa özgü sağkalım:</b>	<b>76</b>	<b>86</b>	<b>100</b>	<b>24</b>
<b>5-7-10 yıl</b>	<b>74</b>	<b>82</b>	<b>90</b>	<b>12</b>
	<b>70</b>	<b>82</b>	<b>90</b>	<b>22</b>





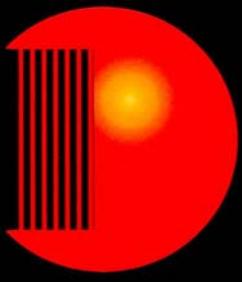
# EVRE

- T1: Böbreğe sınırlı 7 cm'den küçük tümör
  - T1a: 4 cm'den küçük
  - T1b: 4-7 cm
- T2: Böbreğe sınırlı 7 cm'den büyük tümör
- T3: Ana venlere uzanan veya doğrudan adrenal invazyonlu veya perinefrik veya renal sinüs yağ dokuya invaze, Gerota fasiasını aşmayan tümör
  - T3a: Adrenal veya perinefrik veya sinüs yağ doku invazyonlu
  - T3b: Makroskopik diyafragma altı renal ven veya vena kava veya duvarlarına invazyonlu
  - T3c: Diyafragma üzeri vena kava veya duvarına invazyonlu
- T4: Gerota fasiasını geçmiş tümör



# EVRE

- TNM 1997 2.5-7 cm
- TNM 2004 4-7 cm
  - Nefron koruyucu cerrahi
- T3a:
  - Adrenal metastazı (daha kötü prognozlu)
  - Perinefrik-sinüs yağ doku invazyonu
- I, II, III, IV: %91,74, 67, 32



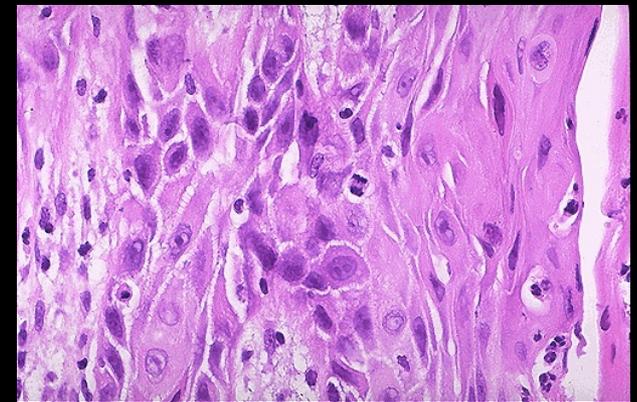
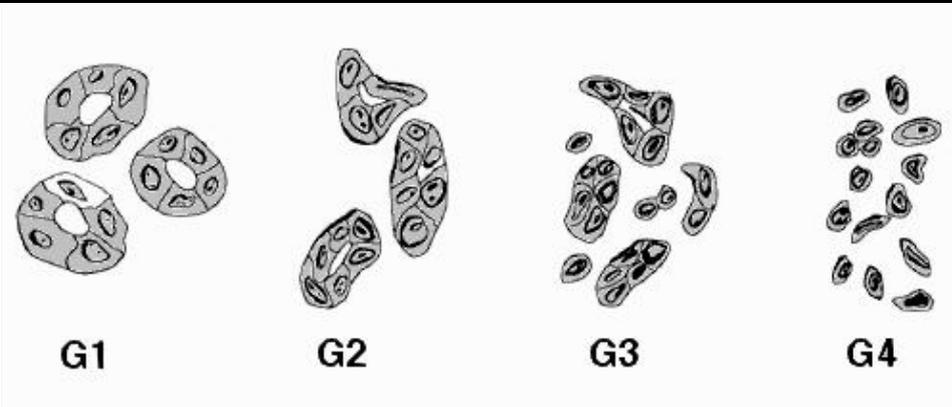
# DERECE

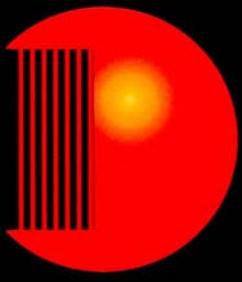
Belirlemesi gereken gruplar:

- Cerrahi tedavi sonrası hastaliksız olanlar,
- Metastaz olanlar,
- Arada kalanlar. . .

# DERECE

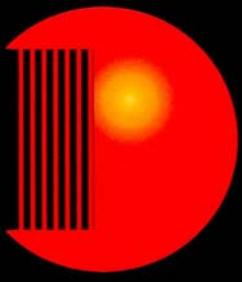
- Sınır noktaları
- Heterojenite
- Doku takibi
- Farklı türler: aynı derecelendirme s.
- Fuhrman: Nükleus/nükleol





# DERECE

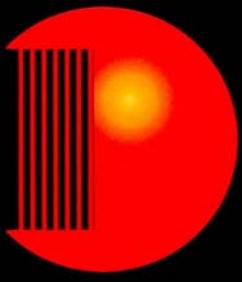
Sistem	Evre	Olgu	Anlam	Sağkalım
Fuhrman	1-4	85	1, 2+3, 4	1, 2+4
Medeiros	1-4	121	1+2, 3, 4	1+2, 3+4
Gelb	1	82	1+2, 3+4	1+2, 3+4
Grignon	1-4	103	1+2, 3, 4	1+2, 3+4
Green	1	55		1+2+3, 4
Störkel	1-4	797	1, 2, 3	1, 2+3



# DERECE

- Tüm sistemler prognostik
- Metastaz/lokal nüks, evre, yaşam süresi ile ilişkili
- PCNA, evre, AgNOR'dan bağımsız değil!



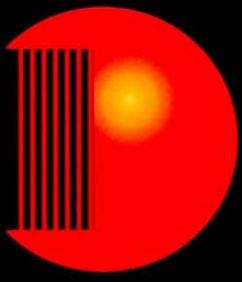


# PROGNOZ

130 olgu

- Tümör çapı "continous" deęişken olarak prognostik
- Fuhrman derecesi ve AgNOR da prognostik
- Sadece tümör çapı baęımsız. . .

Cancer 2002; 94: 658-664

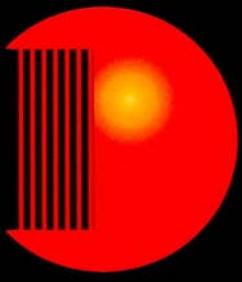


# PROGNOZ

840 olgu

- Tip (berrak → papiller → kromofob)
  - Fuhrman derecesi
  - Tümör çapı
- } • Bağımsız  
• yaşam ve metastaz

Urology 2002; 59: 532-537



# PROGNOZ

405 olgu

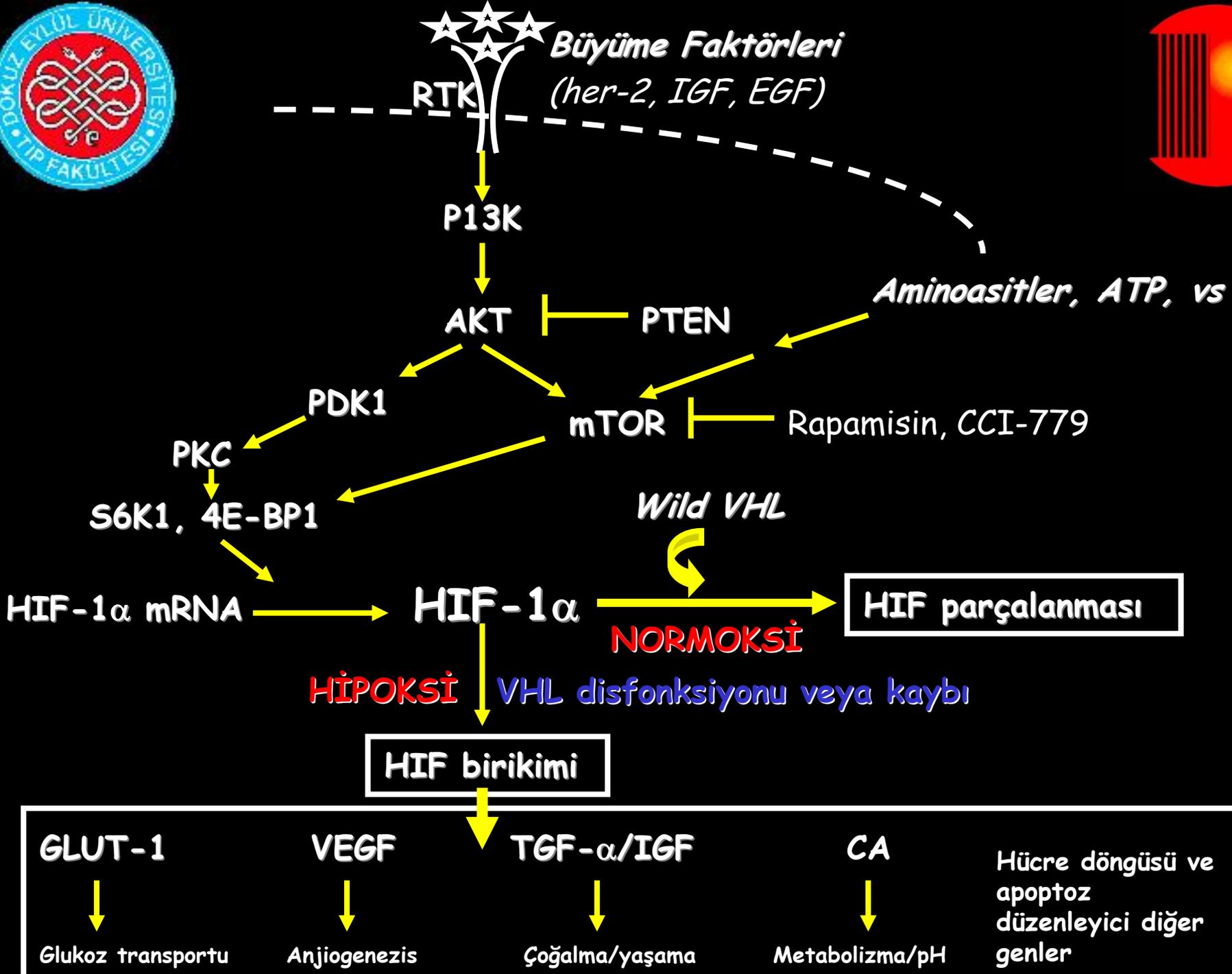
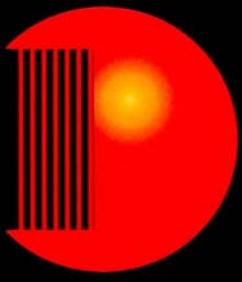
- Tip  
(andiferansiye→sarkomatoid→berrak→papiller→kromofob)
- Evre
- Derece
- Nekroz

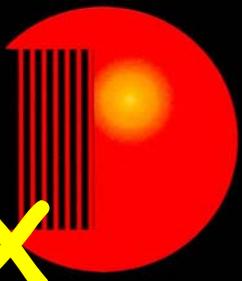
Am J Surg Pathol 2002; 26: 281-291



# PROGNOZ

- DNA ploidi
- Nükleer morfometri
- MIB-1 indeksi
- Anjiogenez
- Lenfovasküler invazyon
- P53, mdm2, cox-2. . .

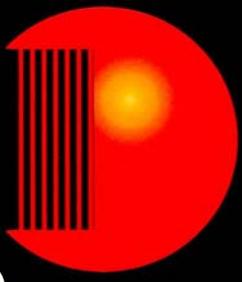




# KARBONİK ANHİDRAZ IX

- RCC  $\uparrow \Rightarrow$  IL-2 cevabı daha iyi
- Normal böbrekte ekspresyon  $\emptyset$
- Papiller ve kromofob RCC  $\downarrow \Rightarrow$  IL-2 cevabı kötü



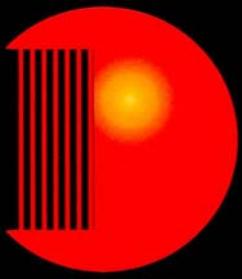


# PREKÜRSÖR LEZYONLAR

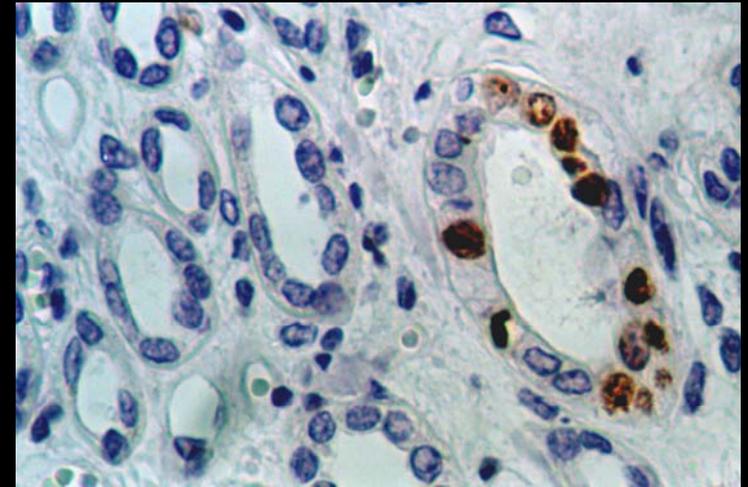
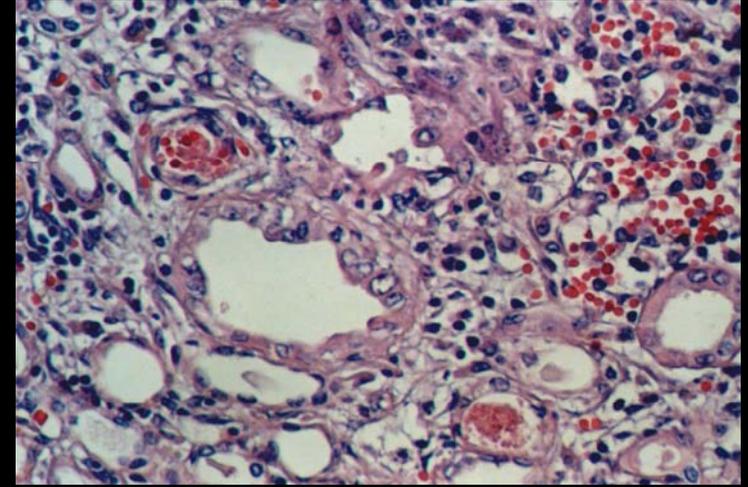
1. Renal displazi/KİS
2. von Hippel-Lindau sendromunda kistlerde displastik deęişiklikler
3. Papiller adenoma
4. Onkositozis
5. Edinsel kistlerde 2 sıradan kalın berrak hücre nodülleri



# RENAL İNTRATUBULER NEOPLAZİ



- Morfoloji
- Yerleşim
- MİK gelişimi
- Yaygınlık, şiddet, sıklık
- Progresyon
- Genetik özellikler



Am J Surg Pathol 1994; 18: 1117-1124

Urology 1999; 53: 684-689

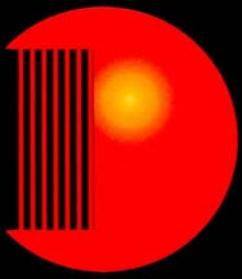


# RENAL İNTRATUBULER NEOPLAZİ

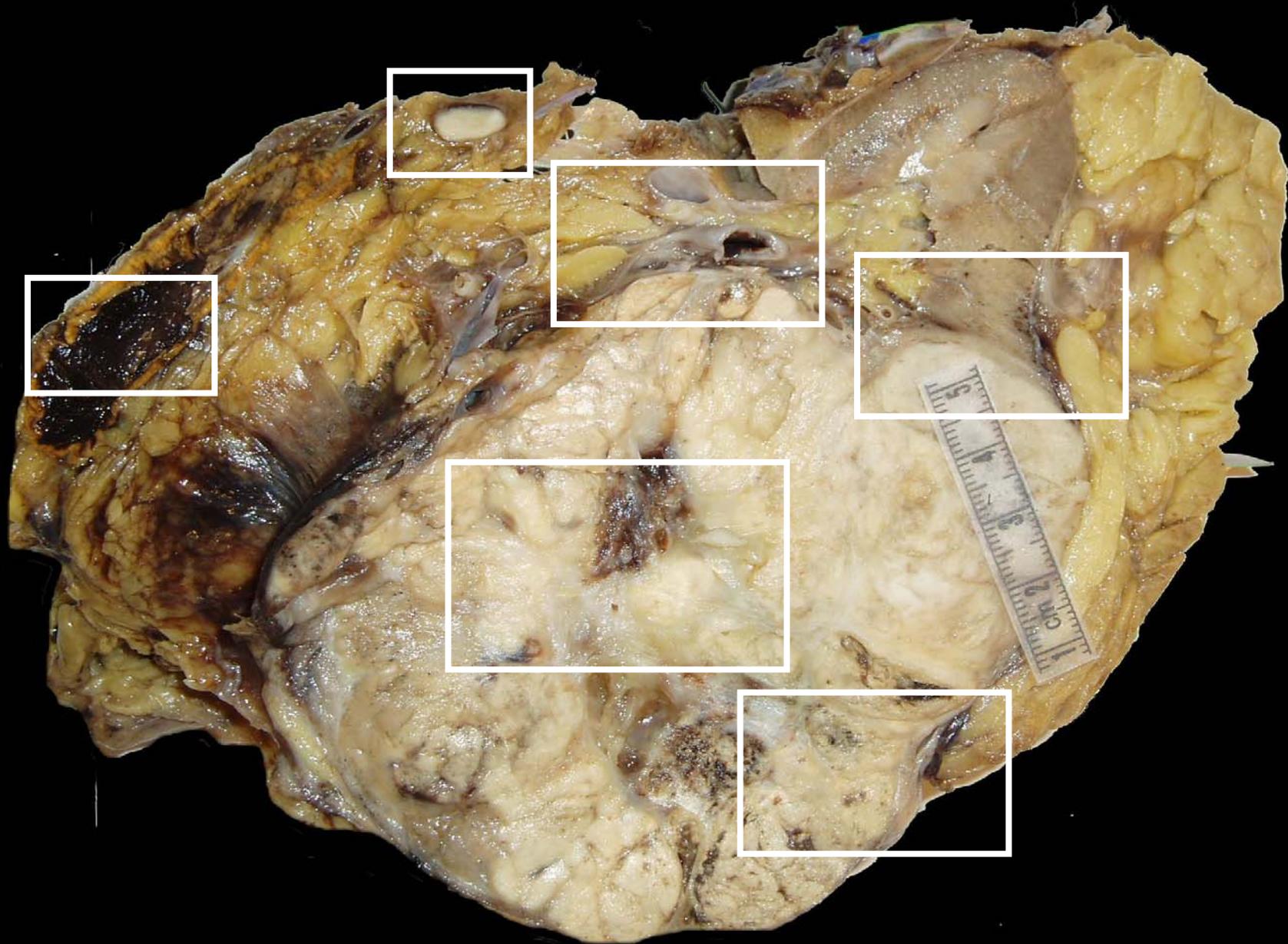
- RHK'da multifokalite %25
- Parsiyel nefrektomi sonrası nüks %0.7-10
- Kontrilateral hastalık %6

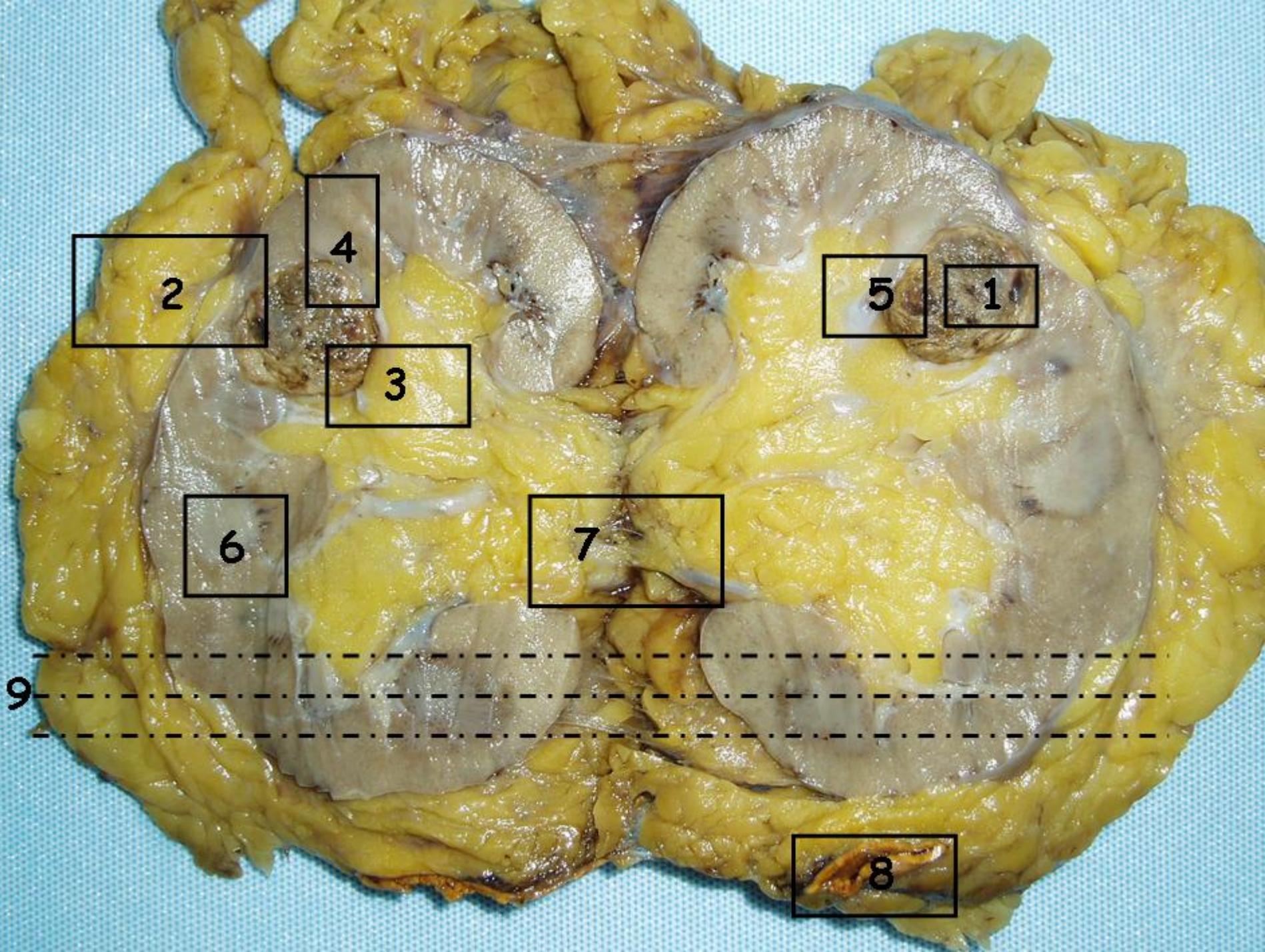


# RENAL İNTRATUBULER NEOPLAZİ



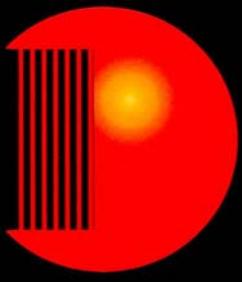
- Morfoloji
- Rapor edilme
- Biopsi ?
- "Management" ?
- Nefron koruyucu cerrahi ?







# RAPOR



- Makroskopik tanımlama, kesitler, bloklar
- Tümör tipi
- Derece (Furhman):
- Patern:
- Tümör çapı:
- Nekroz:
- İnvazyon:
- Renal ven invazyonu:
- Cerrahi sınırlar:
- Nonneoplastik böbrek:
- Adrenal bez:
- Lenfovasküler invazyon:
- Evre:

