

**TİROİD NODÜLLERİNİN SIVI  
BAZLI (*SurePath*)  
SİTOLOJİSİ: 3 Yıllık Histopatolojik  
Korelasyon**

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Patoloji AD, Ankara

Patoloji & Sitopatoloji Kongresi Bursa  
Ekim 2015

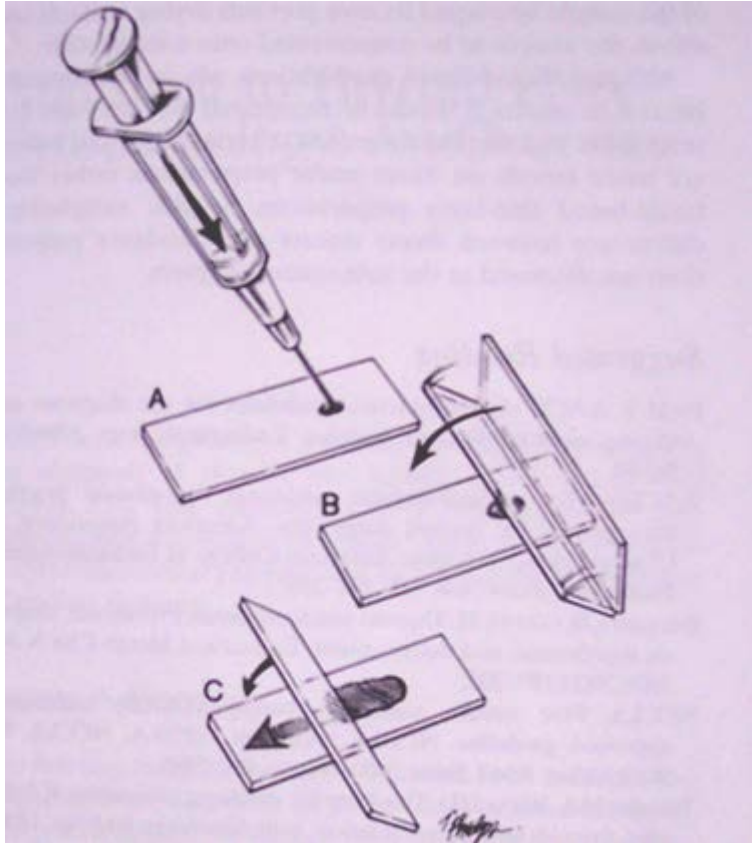
## Sunum

- ❖ Teknik (Özet)
- ❖ Sitoloji Kategorileri-Bethesda Terminolojisi
- ❖ Tiroid FNA: Sitoloji-Olgu Yönetimi
- ❖ Tiroid FNA sitoloji(Klasik Pap- Sıvı Bazlı Sitoloji (SBS / SurePath) Karşılaştırma)
- ❖ Meta-analiz
  - ❖ *SurePath* SBS – Morfoloji korelasyonu
    - ❖ Bethesda Kategorileri (I-II-III-IV,V ve VI)
    - ❖ Morfolojik korelasyonlar ve tuzak olgular
- ❖ Sonuç ve Tartışma

## Ultrasonografi (US) eşliğinde Tiroid İnce İğne Aspirasyonu.



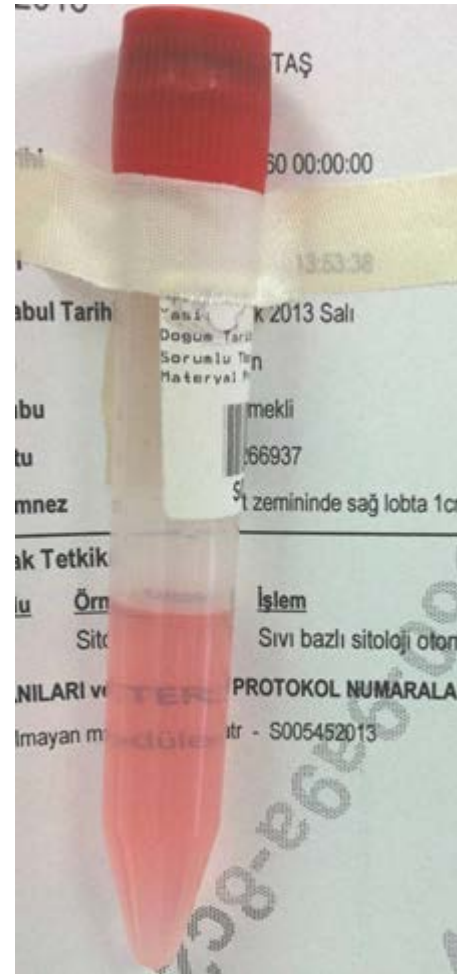
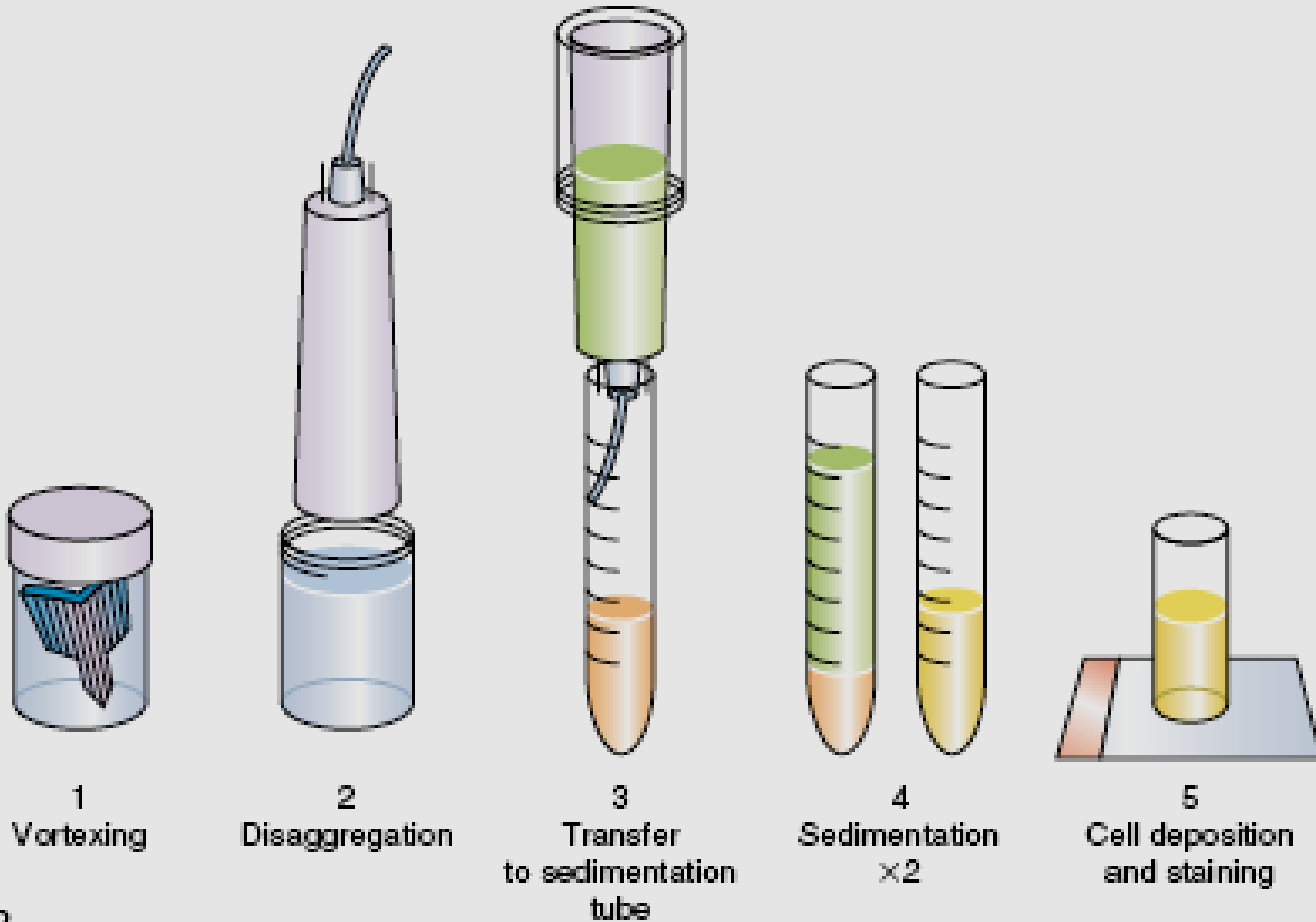
# I. Teknik



Sitolojik preparasyon  
(Klasik metod)



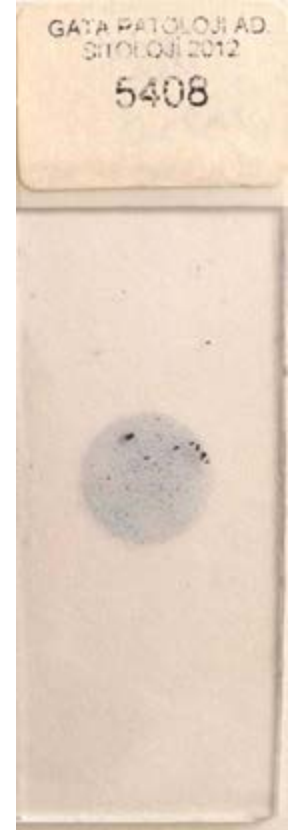
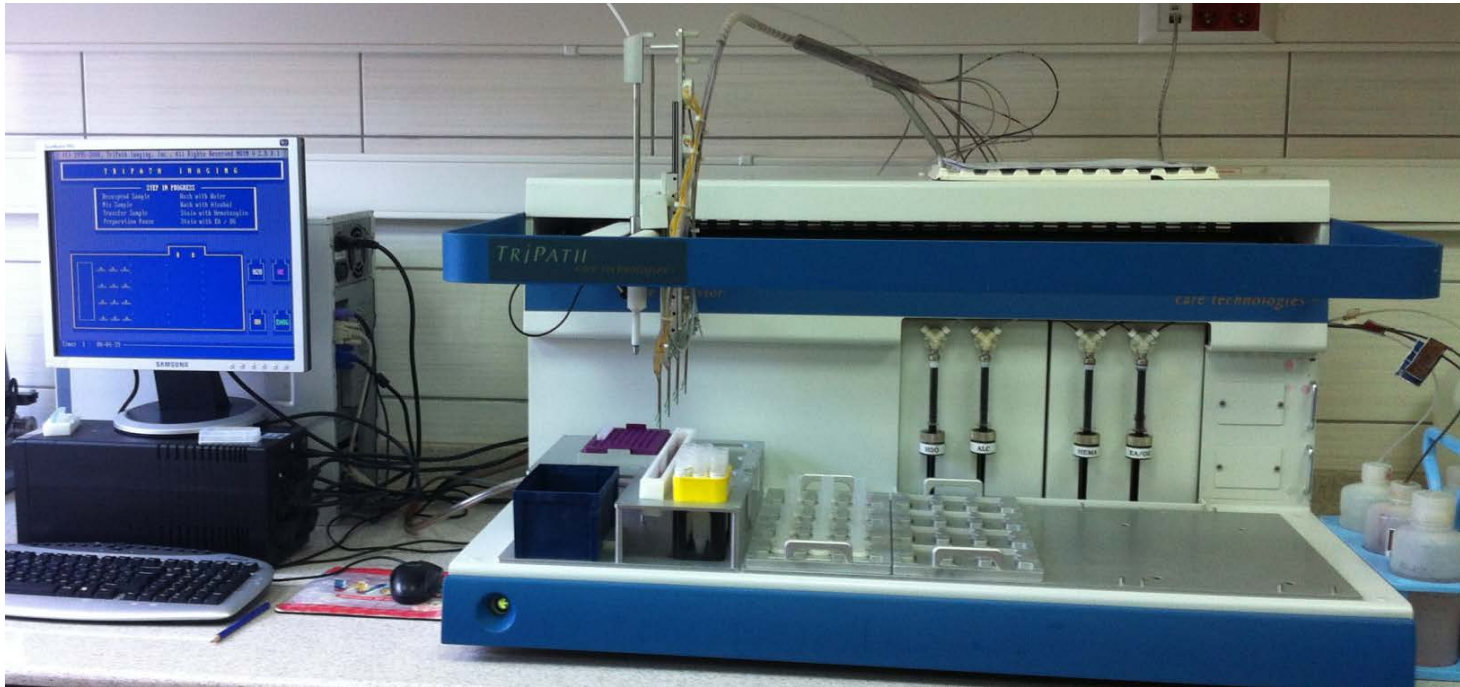
# SurePath (LBC) tekniđi





TriPATH IMAGING  
MATE<sup>™</sup> PREP

TriPATH IMAGING  
Multi-Vol Processor



*SurePath, SBS (LBC) teknik*

# Sitolojik boyalar- teknikler



- *Ethyl alcohol* (%95) fikse – Klasik Papanicolaou boyası
  - Nükleer detaylar (?)
- Romanowsky boyası (Havada-fikse)
- (Giemsa, Diff-quick, May-Grünwald-Giemsa, Wright boyası)
  - Kolloid ve diğer sekresyonlar (sitoplazmik detaylar)
- Carnoy solüsyonu: Eritrosit lizisi (3-5 dakika)
- LBC (SurePath)-Pap boyama:
  - (+CytoRich solüsyonu, eritrosit lizisi)
  - (Berrak nükleer kromatin ve sitoplazmik detaylar)



# Tiroid İİAS'inden Beklentiler

- Spesifik tanısı olan malignite ve antitelerin tanınması
- Hastayı klinik olarak doğru yönlendirecek tanının sağlanması
  - Tıbbi veya Cerrahi tedaviye yöneltme
- Yardımcı tekniklerin (İmmün boyama ve moleküler patoloji vb.) kullanımı

# SİTOLOJİK TANI KATEGORİLERİ

- **Papanicolaou Society of Cytopathology  
(Avrupa-Amerika)**
- **Kanada-Kuzey Amerika**
- **Bethesda Terminolojisi, 2007, 2010 NCI  
(En yaygın)**

## TiIAS Tanı Kategorileri (Eski)

Papanicolaou Society of Cytopathology Task Force on Standards of Practice, 1997 [6]

1. Inadequate/unsatisfactory
2. Benign
3. Atypical cells present
4. Suspicious for malignancy
5. Malignant

Diagnostic Terminology Scheme Proposed by American Thyroid Association, 2006 [7]

1. Inadequate
2. Malignant
3. Indeterminate
  - \_ Suspect for neoplasia
  - \_ Suspect for carcinoma
4. Benign

## Tiroid Sitoloji Kategorileri (Bethesda Terminolojisi, 2010)

- I. Tanısal olmayan/ Yetersiz yayma
- II. Benign
- III. Önemi belirsiz Atipi (AUS) /  
“ “ Folliküler Lezyon (FL-US)
- IV. Folliküler Neoplazm / Neoplazm olasılığı  
(Hürthle hücreli dahil)
- V. Malignite Şüphesi / Malignite olasılığı
- VI. Malign

# Tiroid (İİA) Sitoloji Kategorileri (BETHESDA Terminolojisi)

## I. Tanısal olmayan / Yetersiz yayma

- Hiposellülarite/Suboptimal sellülarite (*non-diagnostic, unsatisfactory*)

## II. Benign

- Benign Folliküler Nodül, Nodüler Guatr, Tiroidit, vb

## III. Önemi belirsiz Atipi (AUS) / Folliküler Lezyon (FL-US)

- Belirsiz, Indeterminate grup

## IV. Folliküler Neoplazm / Neoplazm şüphesi (FN/FN?)

- (+ Hürthle hücreli neoplazm)

## V. Malignite şüphesi (Hiposellülarite; genellikle papiller ve medüller karsinoma için)

- FvPTK, Kistik PTK, Hyalinize trabeküler tumor vb.

## VI. Malign

- *Primer ve metastatik maligniteler*

## Tiroid sitolojilerinin Bethesda Kategorilerine göre dağılımı, olgu yönetimi ve malignite riskleri

BETHESDA KATEGORİLERİ (2010)	Tiroid Sitolojileri	Öneri	Malignite riski
I. Tanısal olmayan / Yetersiz yayma	<%10	Tekrar	%1-4
II. Benign	%60	İzlem (6-18 ay)	%0-3
III. Önemi Belirsiz Atipi (AUS) / Foliküler Lezyon (FL-US)	<%7	Tekrar (3-6 ay)	%5-15
IV. Foliküler Neoplazm (FN)/ FN Şüphesi (+Hürthle hücreli)	%10	Lobektomi	%15-30 (%15-45)
V. Malignite Şüphesi	%2-3	Lobektomi + <i>Frozen Section</i> veya Totale yakın tiroidektomi	%60-75
VI. Malign	%3-7	Totale yakın tiroidektomi	%97-99

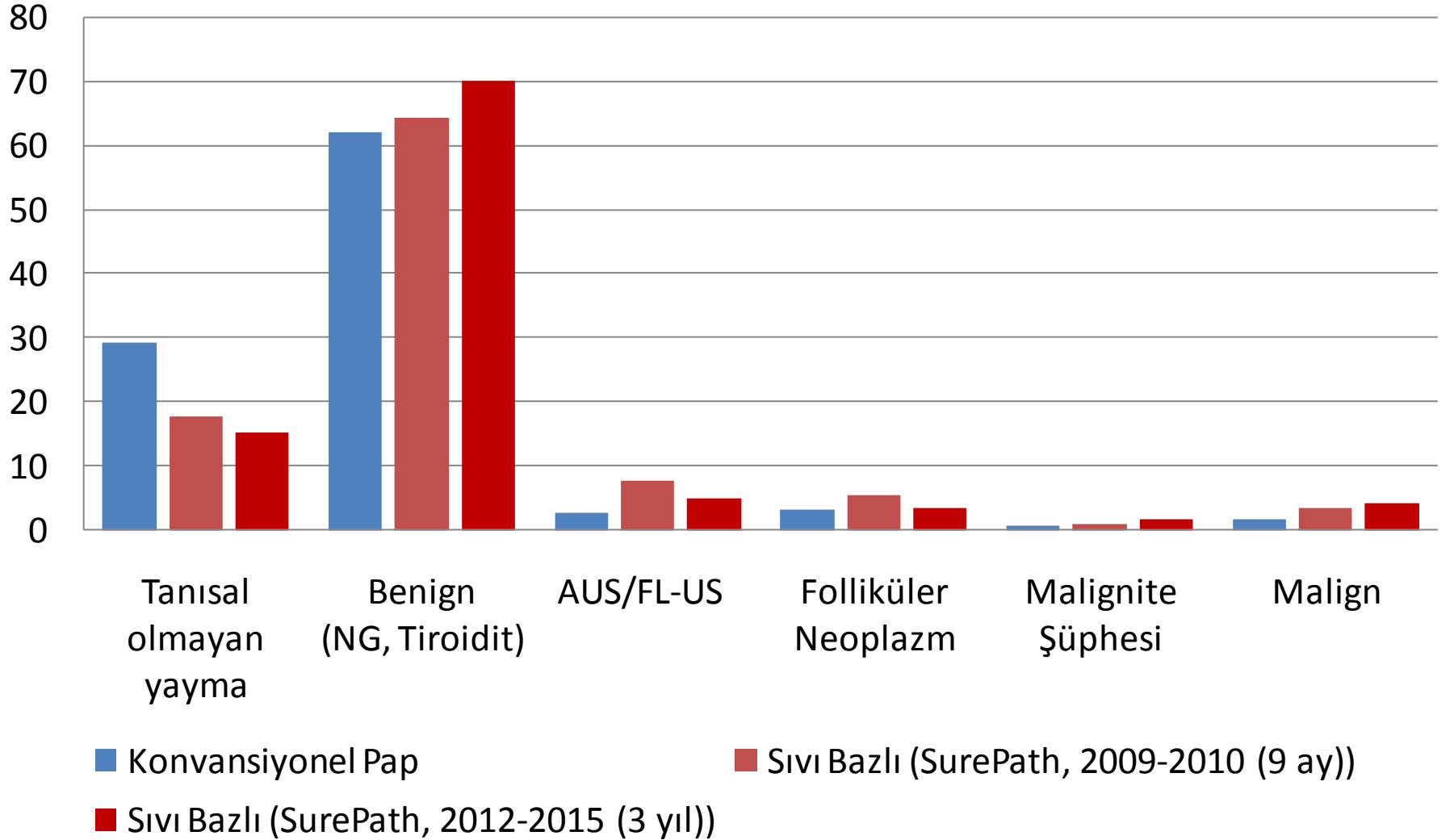
•Ali SZ, Cibas ES. The Bethesda System for Reporting Thyroid Cytopathology. Definitions, criteria and explanatory notes. New York, Springer, 2010.

•Bongiovanni M, et al. The Bethesda System for Reporting Thyroid Cytopathology: a meta-analysis. *Acta Cytol.* 2012;56(4):333-9.

**Tiroid (iiA) Sitoloji-**  
**Konvansiyonel Pap ve Sıvı Bazlı (SurePath) Karşılaştırması**  
**(GATA Patoloji AD)**

<b>Tiroid Sitoloji Kategorileri</b>	<b>2006-2008 (2 yıl) Konvansiyonel Pap</b>	<b>2009-2010 (9 ay) SBS, SurePath</b>	<b>2012-2015 (3 yıl, SBS / SurePath</b>	<b>P değeri</b>
I. Tanısal olmayan	994 (%29.3)	190 (%17.9)	775 (%15.4)	< 0.001
II. Benign (NG, Tiroidit)	2107 (%62.2)	684 (%64.5)	3547 (%70.3)	< 0.001
III. AUS/FL-US (2008 öncesi-Neoplazm dışlanamayan (Rule-out)	96 (%2.8)	82 (%7.7)	249 (%4.9)	< 0.001
IV. Folliküler Neoplazm	107 (%3.2)	59 (%5.5)	170 (%3.4)	< 0.133
V. Malignite şüphesi	26 (%0.8)	10 (%1)	90 (%1.8)	< 0.001
VI. Malign	58 (%1.7)	36 (%3.4)	211 (%4.2)	< 0.001
Toplam	3388 (%100)	1061 (%100)	5042 (%100)	< 0.001

## Konvansiyonel Pap- Sıvı Bazlı Sitoloji (SurePath) Karşılaştırması





## The Bethesda System for Reporting Thyroid Cytopathology: A Meta-Analysis

Massimo Bongiovanni<sup>a</sup> Alessandra Spitale<sup>a</sup> William C. Faquin<sup>b</sup>  
Luca Mazzucchelli<sup>a</sup> Zubair W. Baloch<sup>c</sup>

<sup>a</sup>Institute of Pathology, Locarno, Switzerland; <sup>b</sup>Massachusetts General Hospital, Boston, Mass., and  
<sup>c</sup>University of Pennsylvania Medical Center, Philadelphia, Pa., USA

### Cytohystological correlations in the 6-tiered Bethesda System

**Table 3.** Cytohystological correlations in the 6-tiered Bethesda System

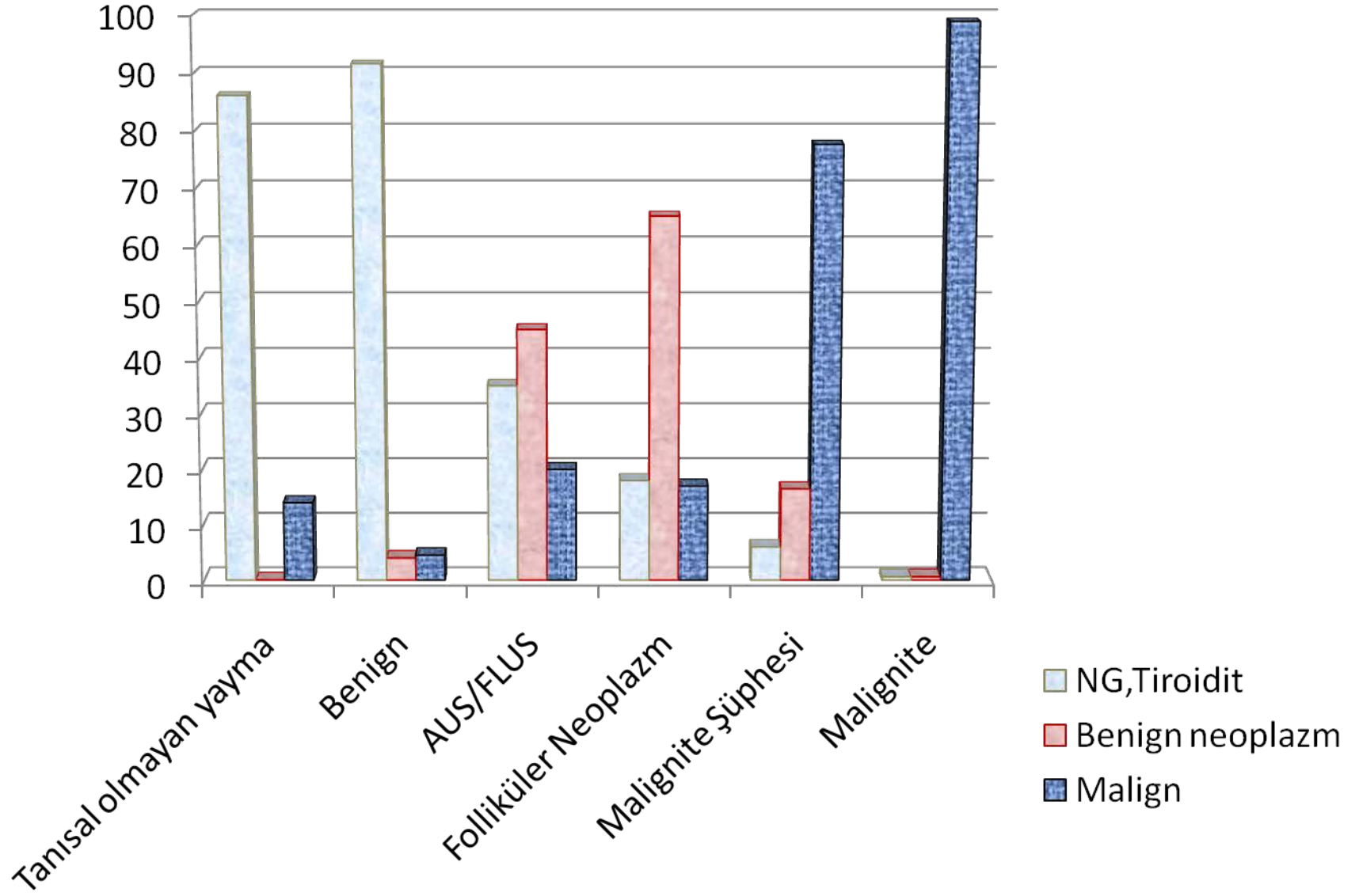
Cytological diagnosis	All FNAs		All FNAs with histological follow-up			Benign histology		Malignant histology	
	n	% total	n	% total <sup>a</sup>	% category <sup>b</sup>	n	% <sup>c</sup>	n	% <sup>c</sup>
Nondiagnostic	3,271	12.9	530	8.3	16.2	441	83.2	89	16.8
Benign	15,104	59.3	1,563	24.6	10.4	1,505	96.3	58	3.7
AUS/FLUS	2,441	9.6	957	15.0	39.2	805	84.1	152	15.9
FN/SFN	2,571	10.1	1,791	28.2	69.7	1,323	73.9	468	26.1
Suspicious for malignancy	680	2.7	501	7.9	73.7	124	24.8	377	75.2
Malignant	1,378	5.4	1,020	16.0	74.0	14	1.4	1,006	98.6
Total	25,445	100	6,362	100	25.0	4,212	66.2	2,150	33.8

<sup>a</sup> Percentage of the 6,362 cases with follow-up. <sup>b</sup> Percentage of cases operated in each DC. <sup>c</sup> Percentage of cases calculated of the total number of operated cases in each category.

Cytological diagnosis	All FNAs		2012-2015 (3 yıl) SBS, SurePath (GATA Patoloji AD)	
	n	% total		
Nondiagnostic	3,271	12.9	<b>775</b>	<b>(%15.4)</b>
Benign	15,104	59.3	<b>3547</b>	<b>(%70.3)</b>
AUS/FLUS	2,441	9.6	<b>249</b>	<b>(%4.9)</b>
FN/SFN	2,571	10.1	<b>170</b>	<b>(%3.4)</b>
Suspicious for malignancy	680	2.7	<b>90</b>	<b>(%1.8)</b>
Malignant	1,378	5.4	<b>211</b>	<b>(%4.2)</b>
<b>Total</b>	<b>25,445</b>	<b>100</b>	<b>5042</b>	<b>(%100)</b>

Tiroid Sıvı Bazlı (SurePath) Sitolojisi ve histopatolojik korelasyon  
(2012-2015; 3 yıl, GATA Patoloji AD)

Sitoloji		Histopatoloji			
Bethesda Kategorileri		Tiroidektomi	Nodüler Guatr, tiroidit	Benign Neoplazm	Malign
I. Tanısal olmayan	<b>775 (%15.4)</b>	14 (%2)	12 (%86)	-	2 (%14)
II. Benign	<b>3547 (%70.3)</b>	129 (%3.5)	118 (%91.5)	5 (%4)	<b>6 (%4.5)</b>
III. AUS/FL-US	<b>249 (%4.9)</b>	20 (%8)	7 (%35)	9 (%45)	4 (%20)
IV. Neoplazm (FN/HN)	<b>170 (%3.4)</b>	78 (%46)	14 (%18)	<b>51 (%65)</b>	<b>13 (%17)</b>
V. Malignite Şüphesi	<b>90 (%1.8)</b>	67 (%74.5)	4 (%6)	11 (%16.5)	<b>52 (%77.5)</b>
VI. Malign	<b>211 (%4.2)</b>	171 (%81)	1 (%0.6)	1 (%0.6)	169 (%98.8)
Toplam	5042 (%100)	499 ( <b>%9.9</b> )	156 (%31.3)	77 (%15.4)	266 ( <b>%53.3</b> )



	All FNAs with histological follow-up			Benign histology		Malignant histology	
	n	% total <sup>a</sup>	% category <sup>b</sup>	n	% <sup>c</sup>	n	% <sup>c</sup>
Nondiagnostic	530	8.3	16.2	441	83.2	89	16.8
Benign	1,563	24.6	10.4	1,505	96.3	58	3.7
AUS/FLUS	957	15.0	39.2	805	84.1	152	15.9
FN/SFN	1,791	28.2	69.7	1,323	73.9	468	26.1
Suspicious for malignancy	501	7.9	73.7	124	24.8	377	75.2
Malignant	1,020	16.0	74.0	14	1.4	1,006	98.6
<b>Total</b>	<b>6,362</b>	<b>100</b>	<b>25.0</b>	<b>4,212</b>	<b>66.2</b>	<b>2,150</b>	<b>33.8</b>

Histopatolojik Korelasyon						
	Tiroidektomi		Benign		Malign	
Tanısal olmayan	14	(%2)	12	(%86)	2	%14
Benign	129	(%3.5)	123	(%95.4)	6	%4.6
AUS/FL-US	20	(%8)	16	(%80)	4	(%20)
FN/ FN?	78	(%46)	65	(%83)	13	(%17)
Malignite şüphesi	67	(%74.5)	15	(%22.5)	52	(%77.5)
Malign	171	(%81)	2	(%1.2)	169	(%98.8)
<b>Toplam</b>	<b>499</b>	<b>%9.9</b>	<b>233</b>	<b>(%46.7)</b>	<b>266</b>	<b>%53.3</b>

**Table 3. Summary of the Meta-Analytic Results Not Mentioned**

Diagnostic Category	Total No. of Studies	Total No. of FNAs With Surgical Follow-Up	Overall Rate of Malignancy (95% CI), %	Heterogeneity Analyses	
				Q	I <sup>2</sup>
AUS/FLUS	47	4474	27 (23-31)	307.24 <sup>a</sup>	85.03
FN/SFN	36	3202	31 (28-36)	146.07 <sup>a</sup>	76.04

# Cancer Cytopathology

## Original Article

**A meta-analytic review of the Bethesda System for Reporting Thyroid Cytopathology: Has the rate of malignancy in indeterminate lesions been underestimated?**

Patrizia Straccia BD<sup>†</sup>, Esther Diana Rossi MDPHd<sup>†</sup>, Tommaso Bizzarro BD, Chiara Brunelli MD, Federica Cianfrini BD, Domenico Damiani MD and Guido Fadda MD\*

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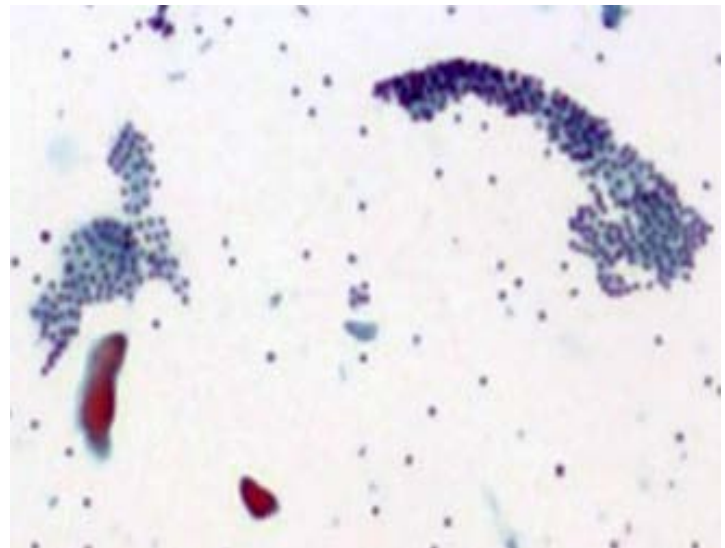
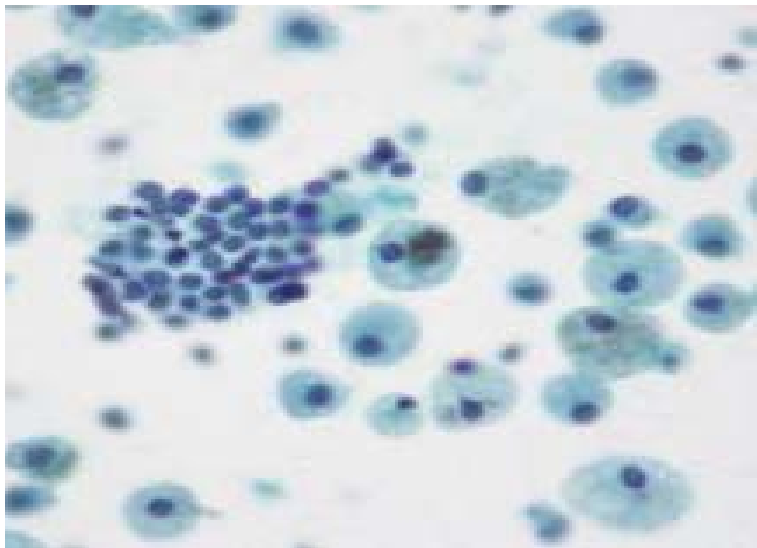
## Issue



Cancer Cytopathology  
Early View (Online Versi  
Record published before  
inclusion in an issue)

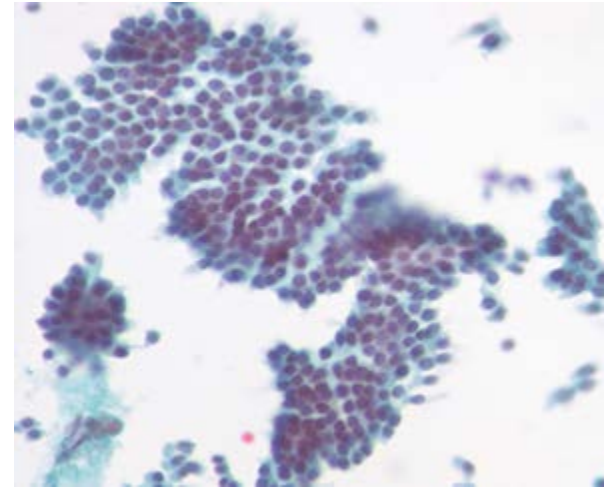
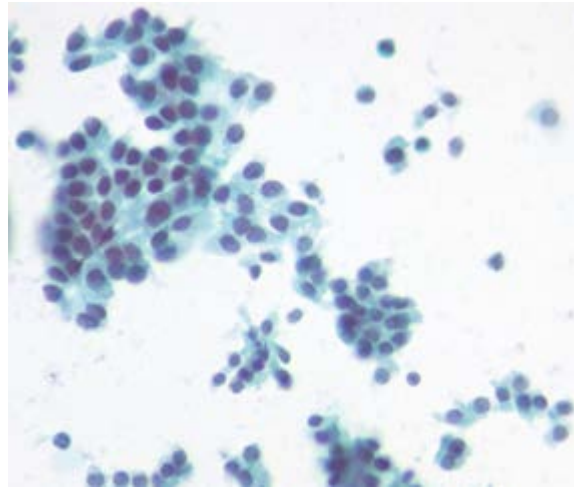
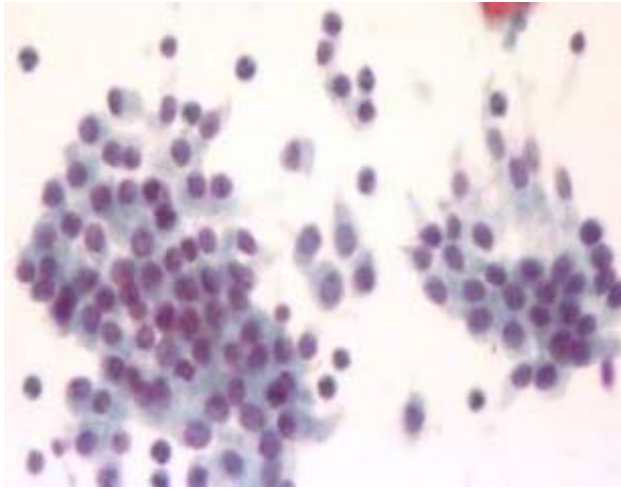
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Bethesda I-II

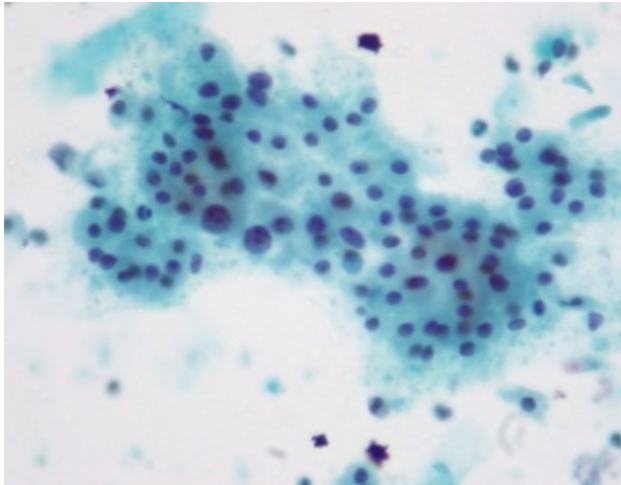


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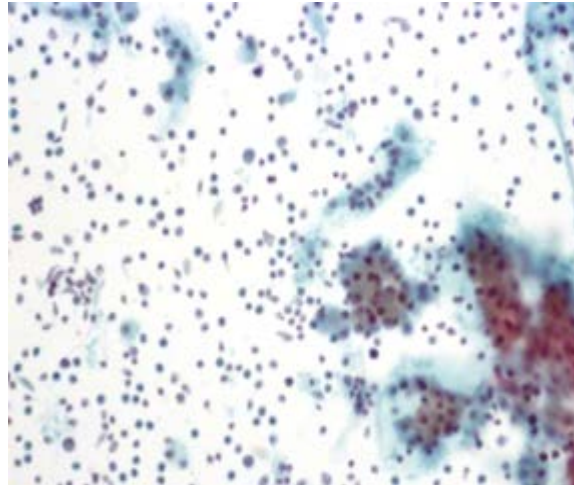
Bethesda II



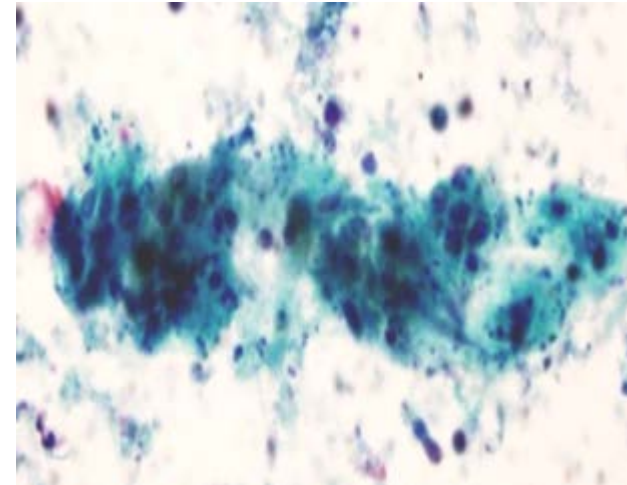
Hiperplastik Guatr Nodülü / BFN



Onkositik metaplazi



Kronik lenfositik tiroidit

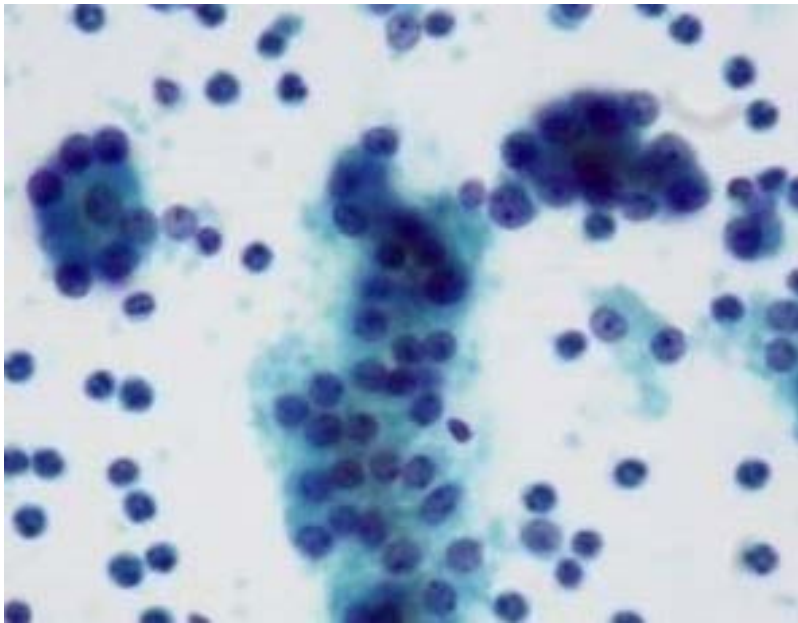


Subakut tiroidit

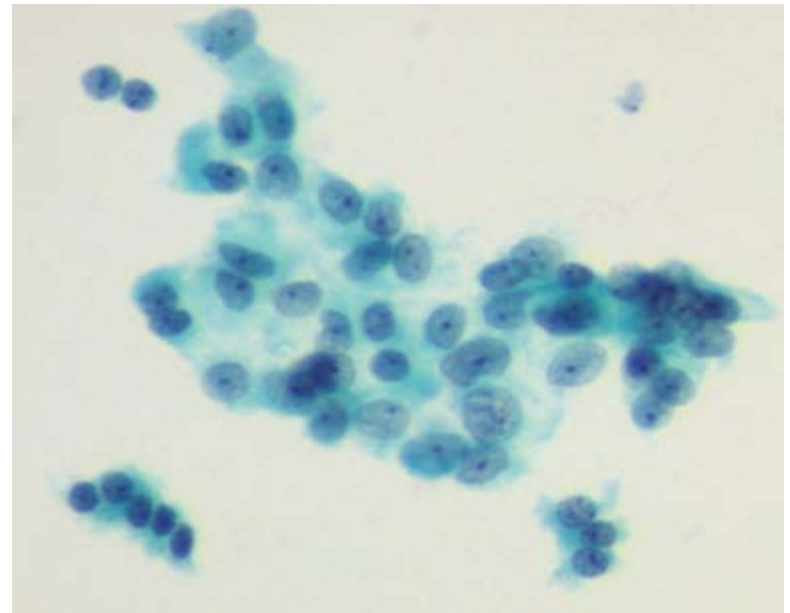


SurePath Sitoloji :

Bethesda III



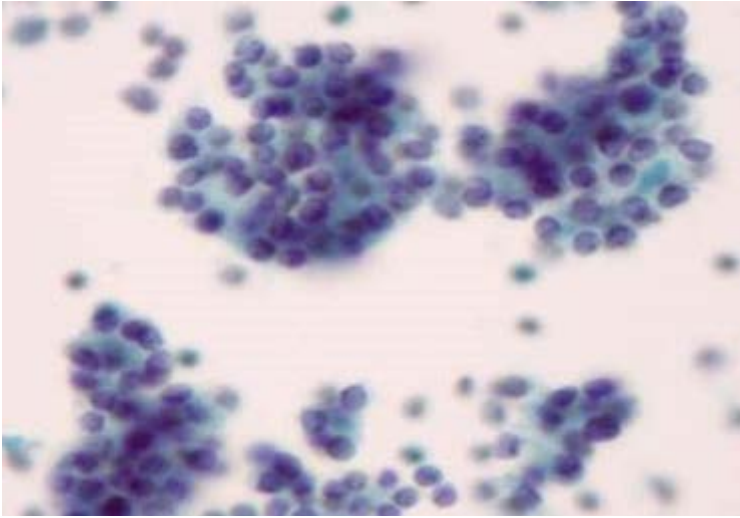
FL-US



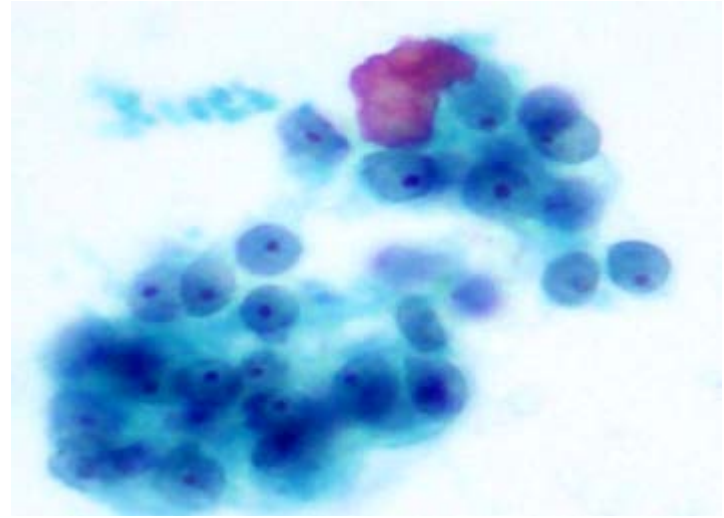
AUS

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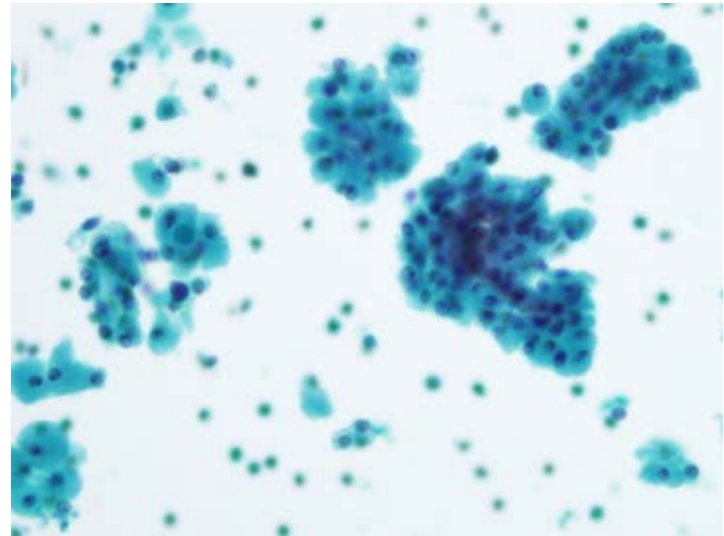
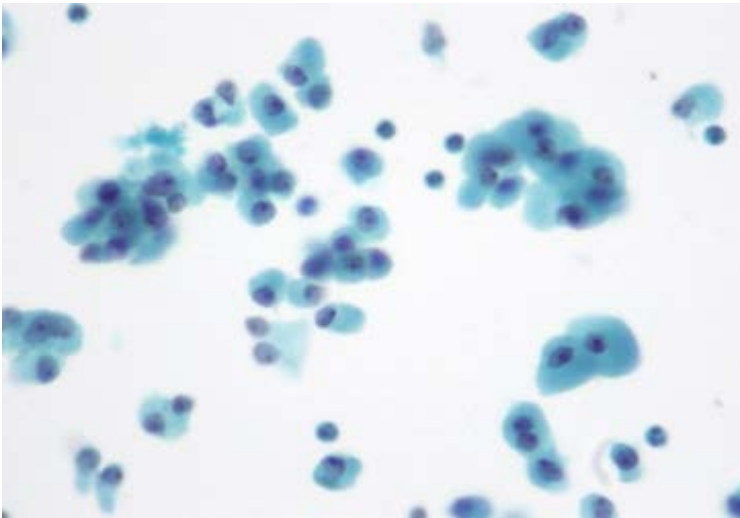
Bethesda IV



FN



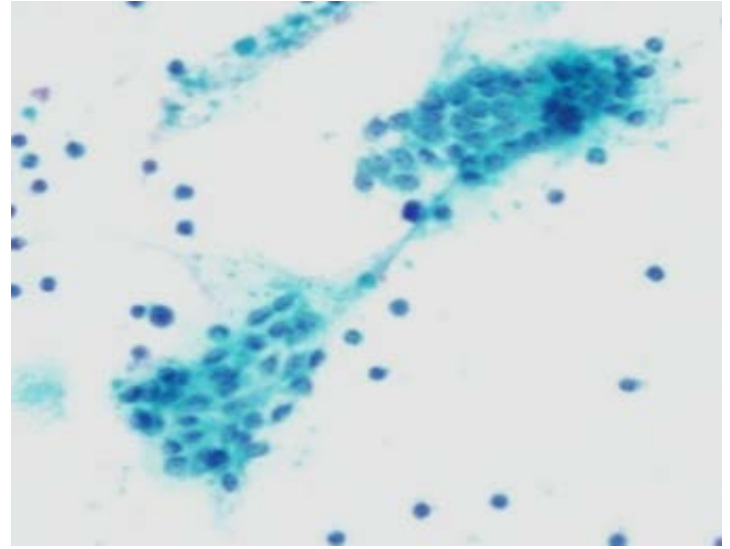
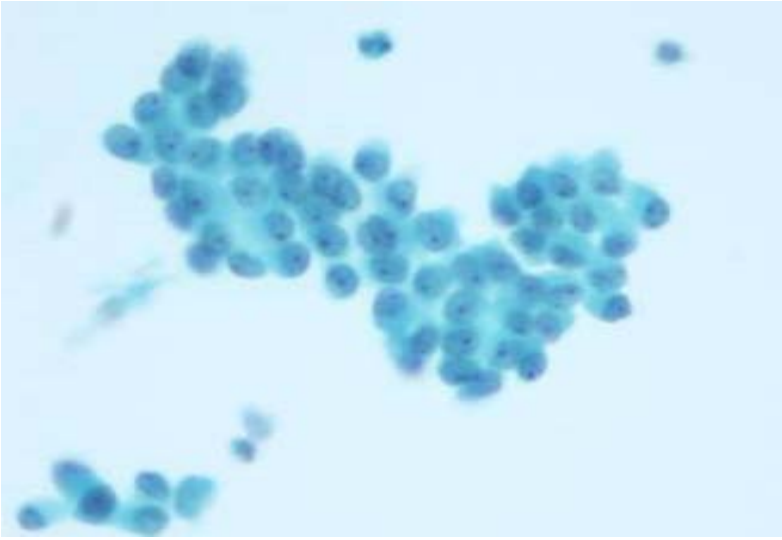
FN



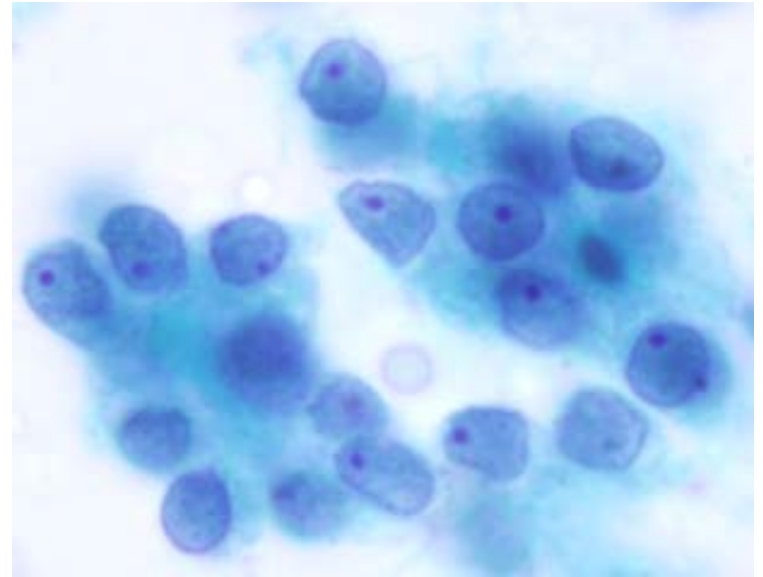
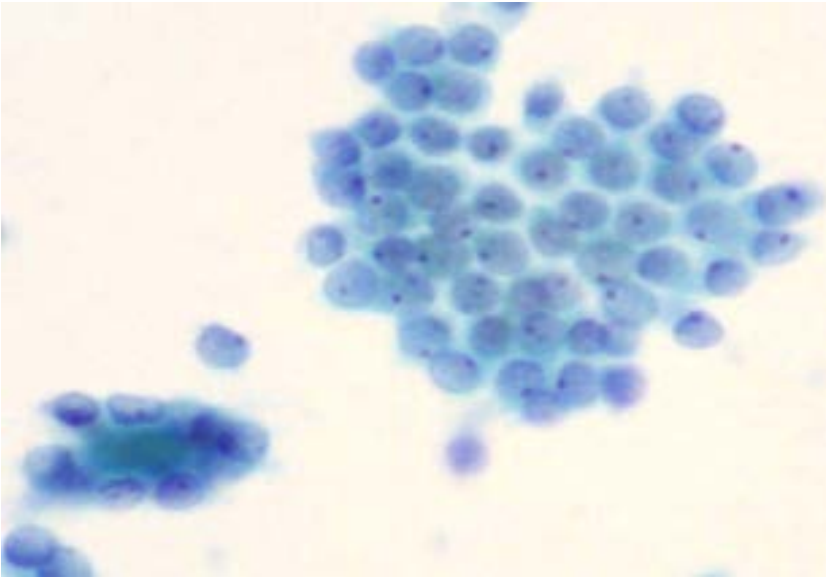
Hürthle hücreli Neoplazm

SurePath Sitoloji :

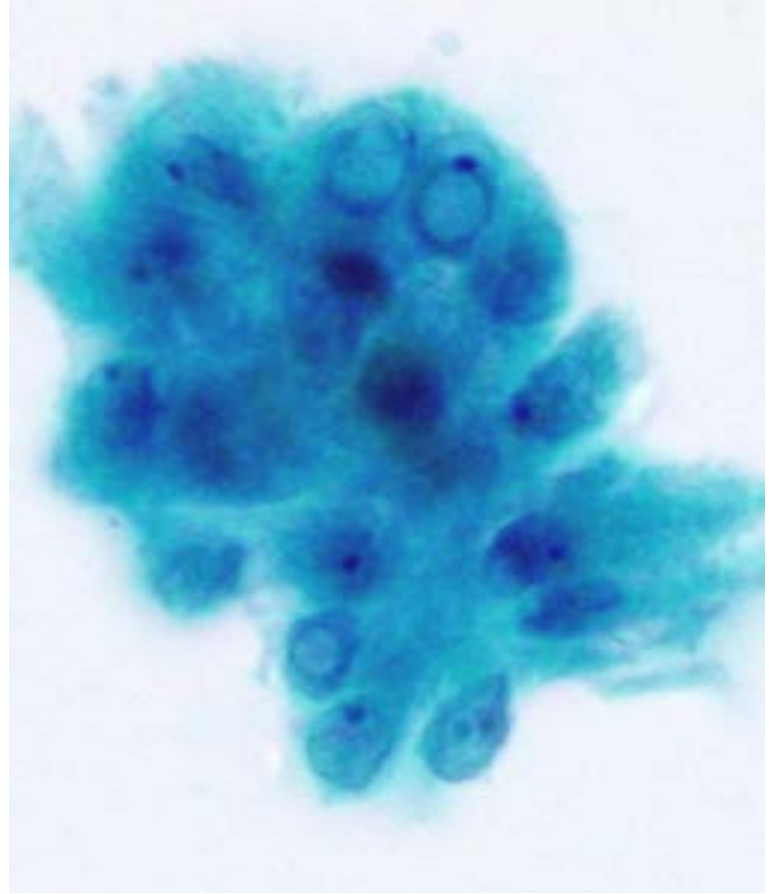
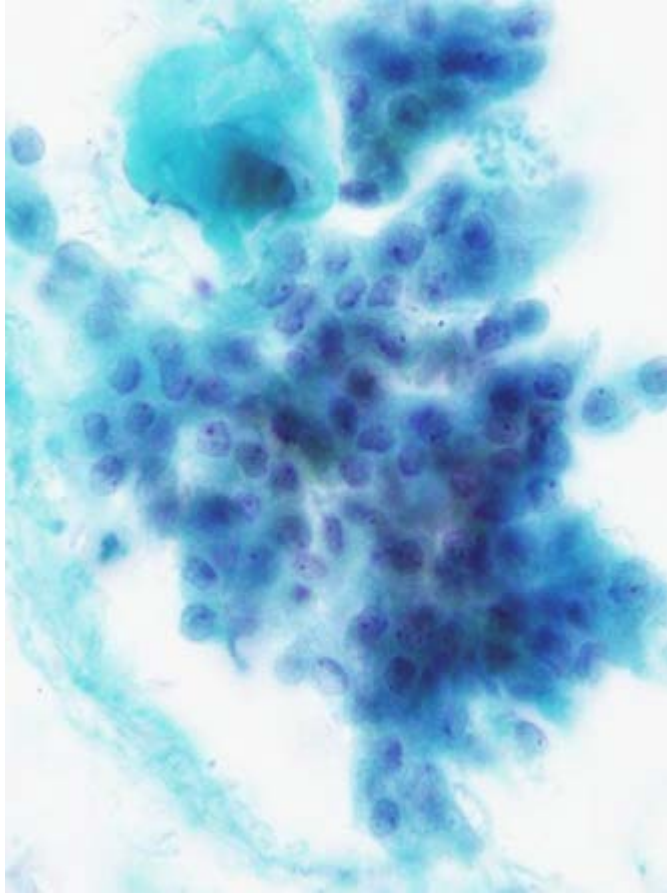
Bethesda V



PTK Şüphesi



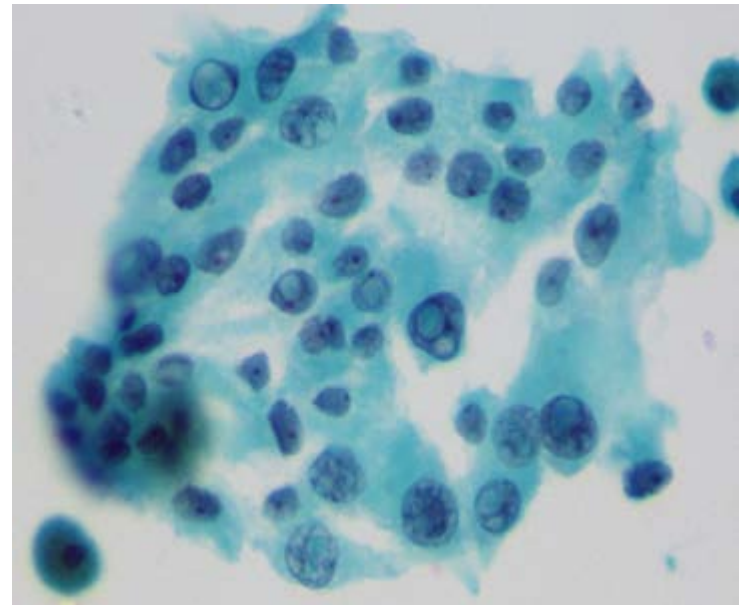
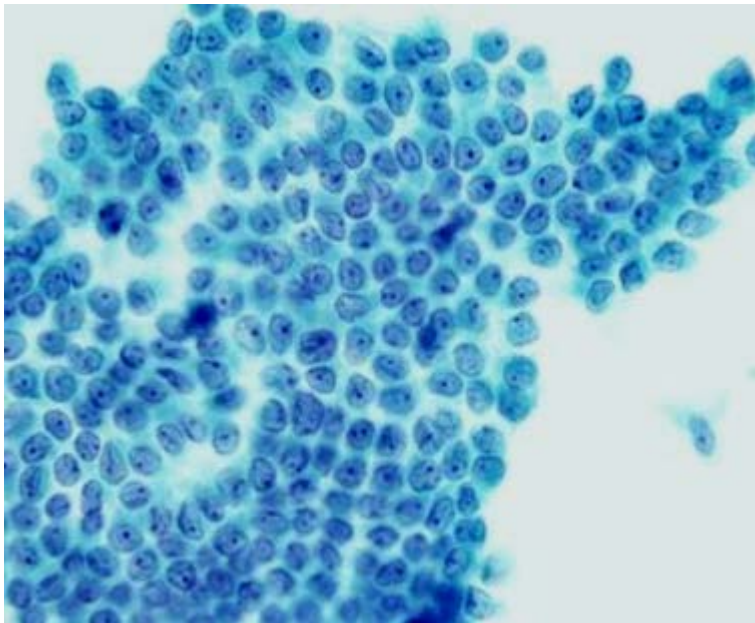
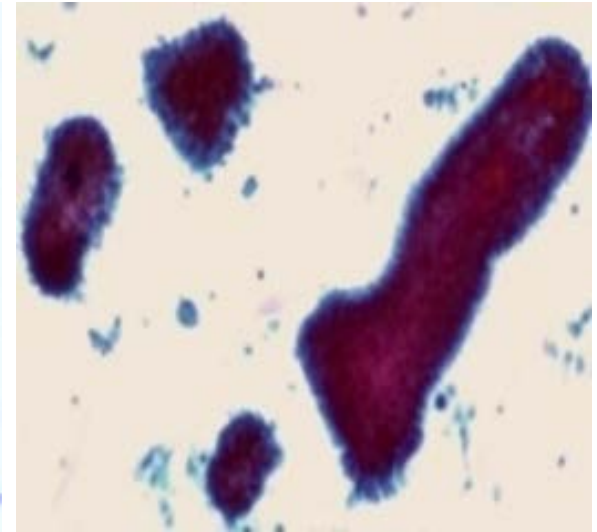
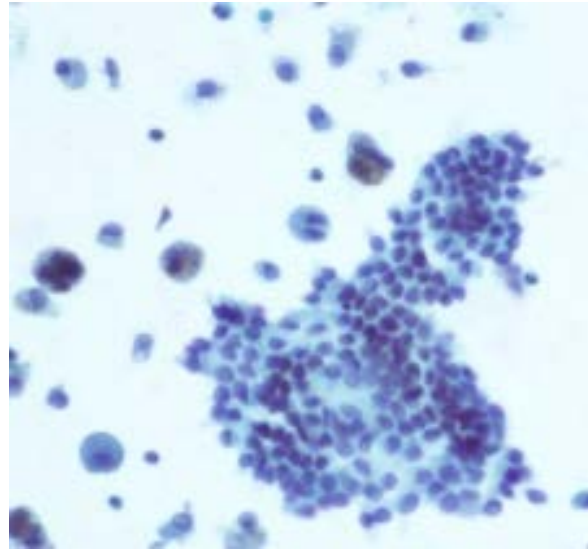
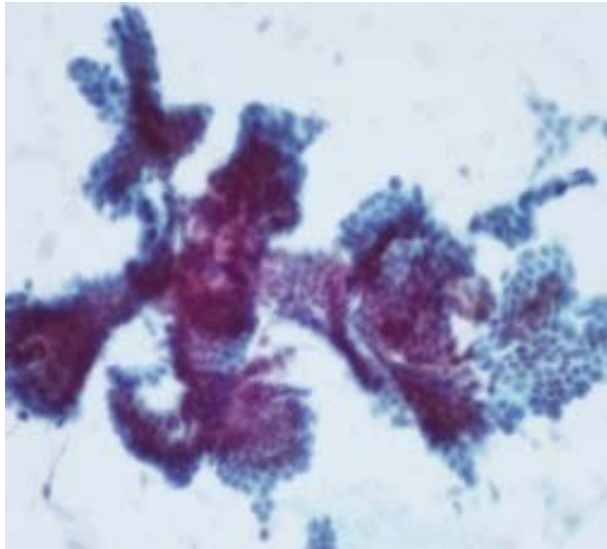
Foliküler varyant PTK Şüphesi



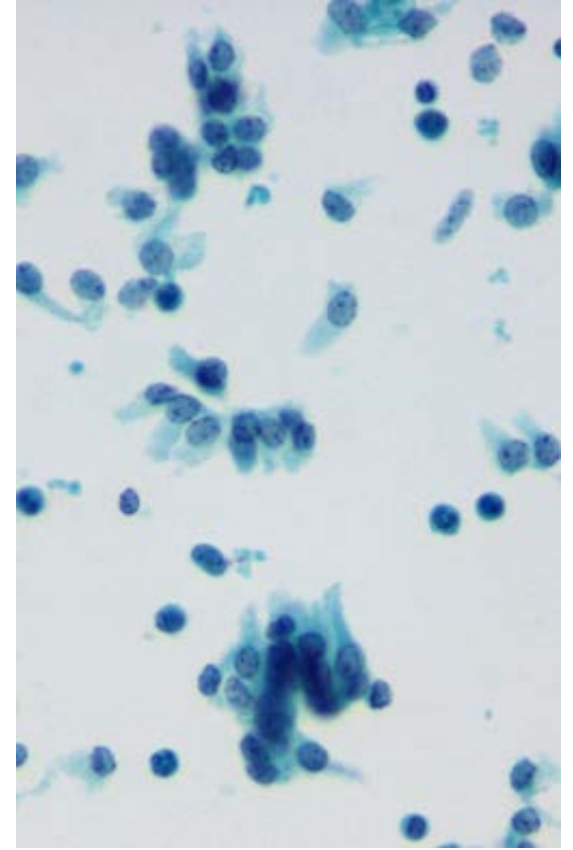
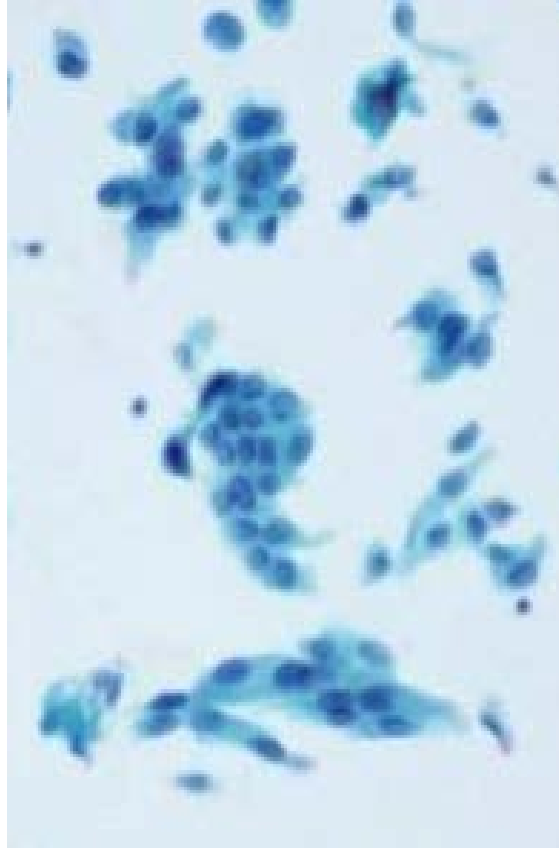
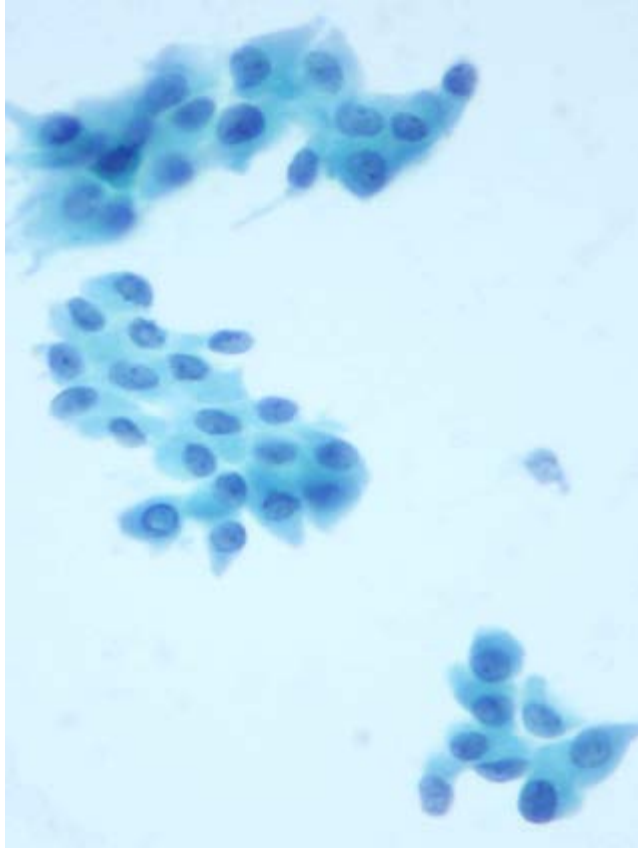
Hyalinize trabeküler tümör

SurePath Sitoloji :

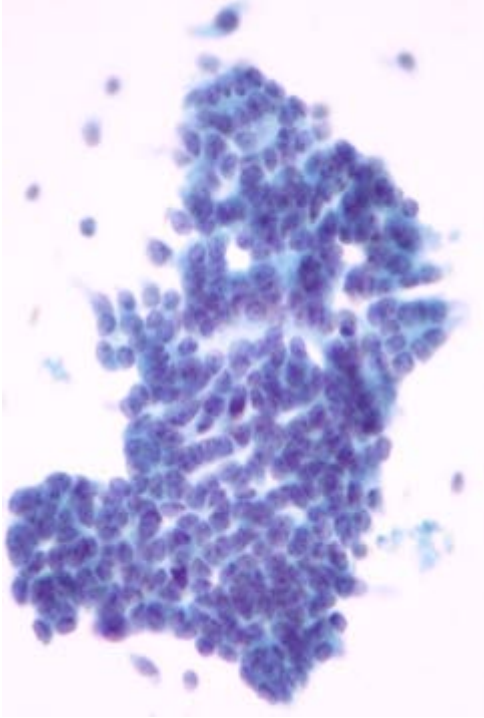
Bethesda VI



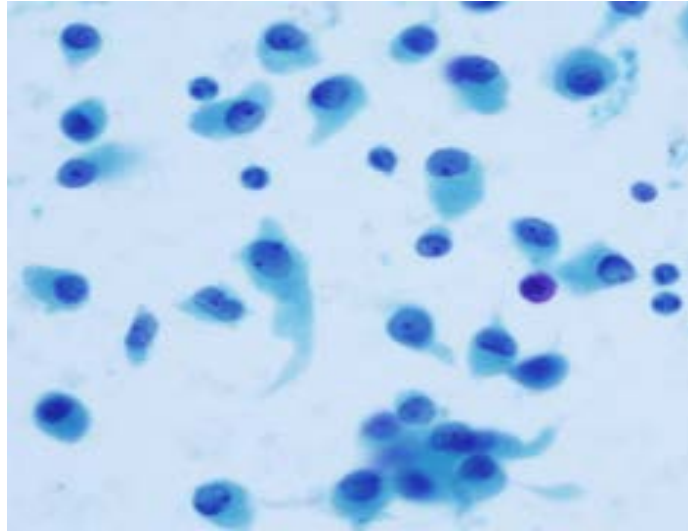
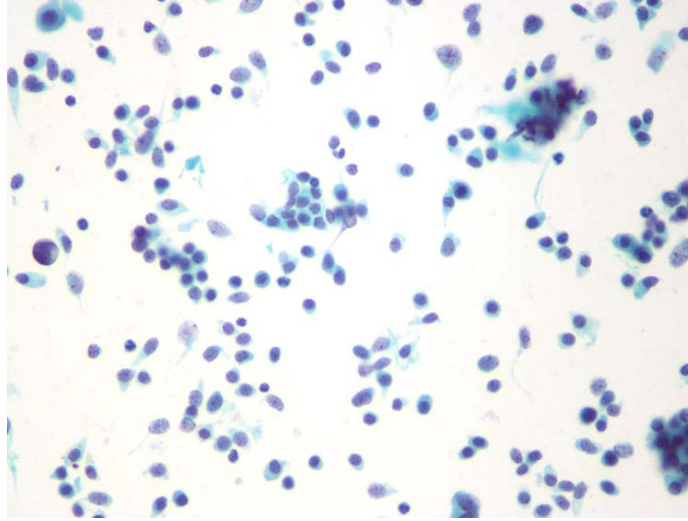
PTK



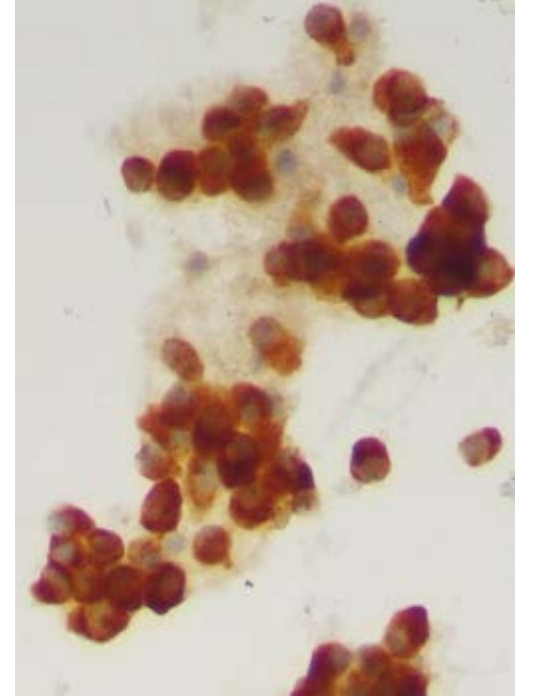
PTK varyantları  
(Onkositik, Uzun hücreli, Kolumnar hücreli)



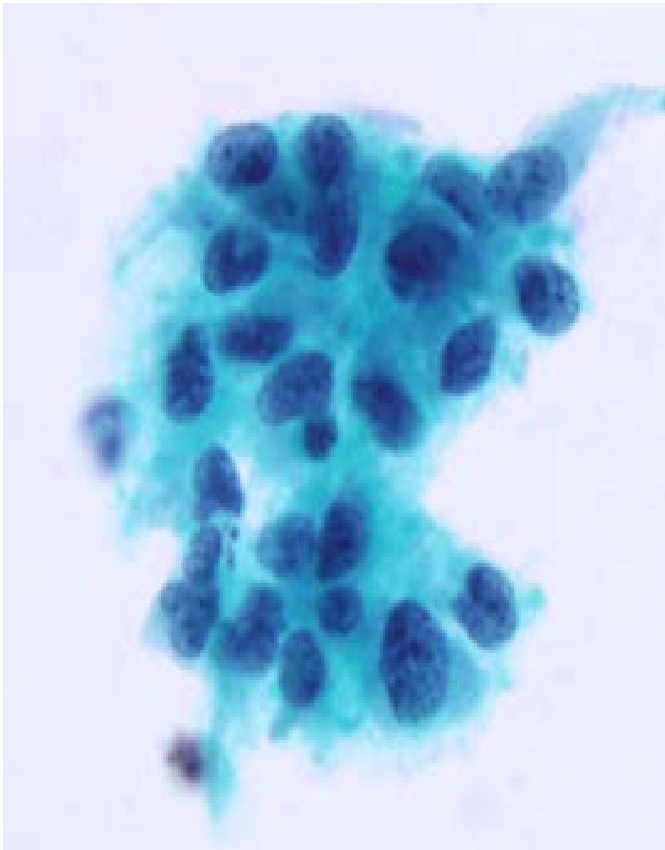
Az diferansiye  
Tiroid Karsinomu



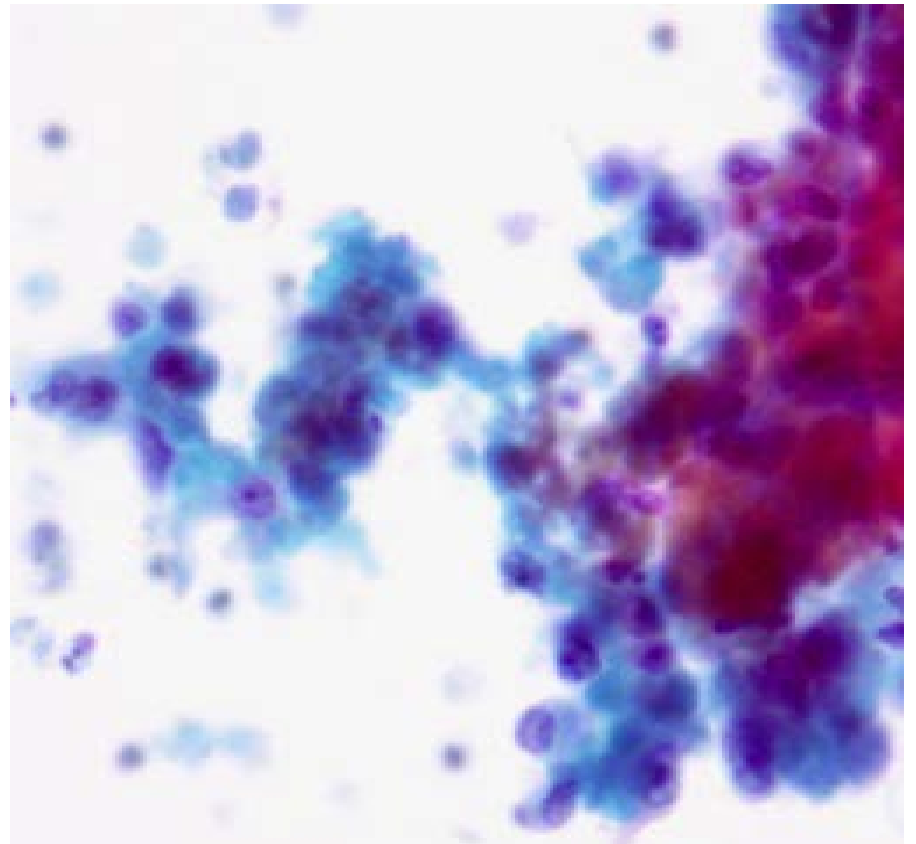
Medüller Karsinoma



Kalsitonin



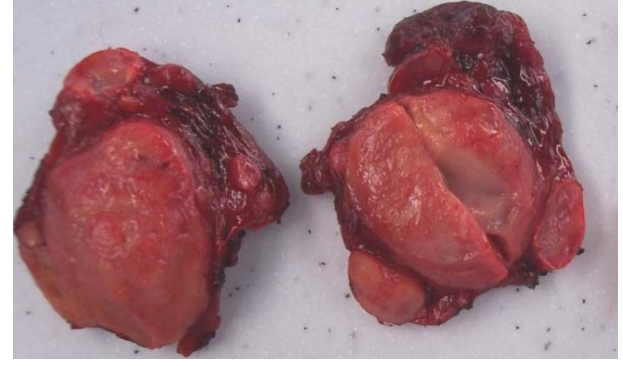
Anaplastik Karsinoma



Anjiyosarkoma



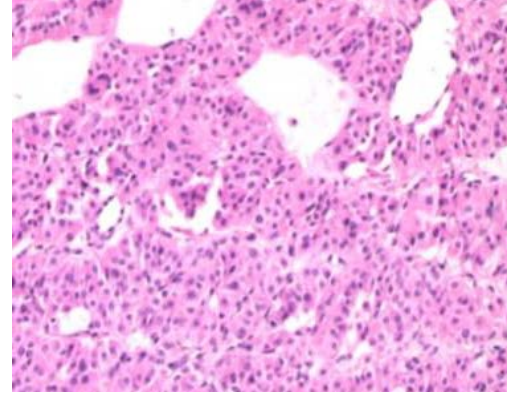
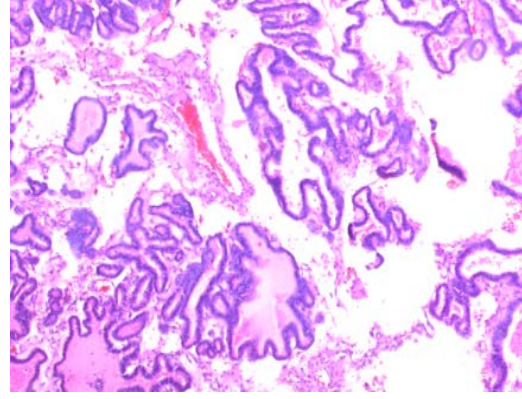
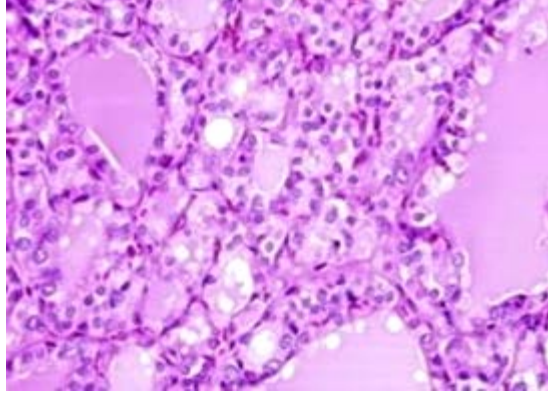
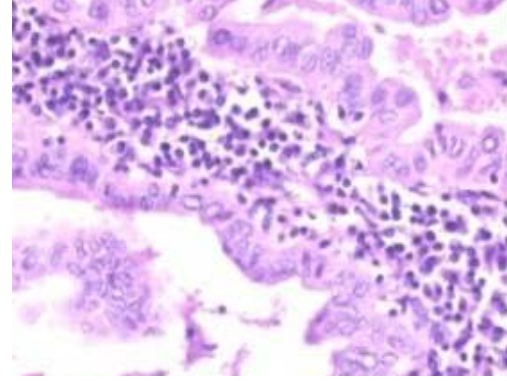
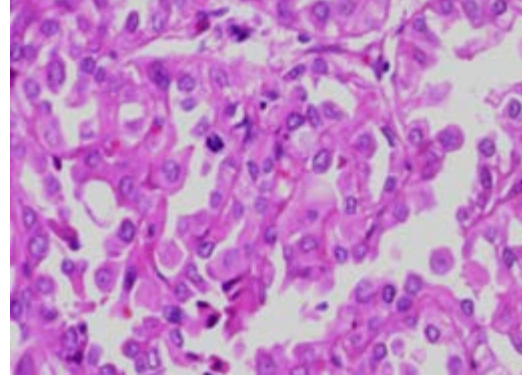
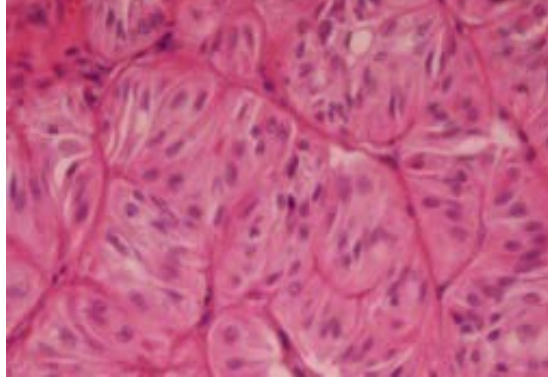
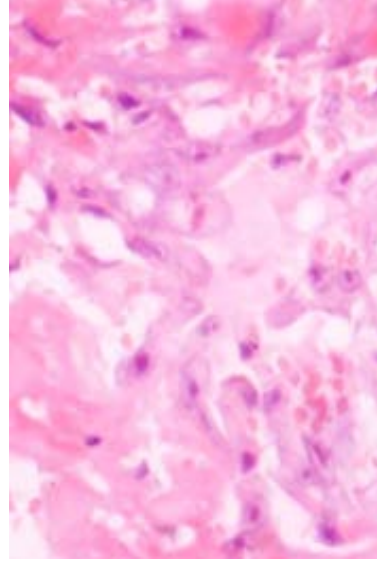
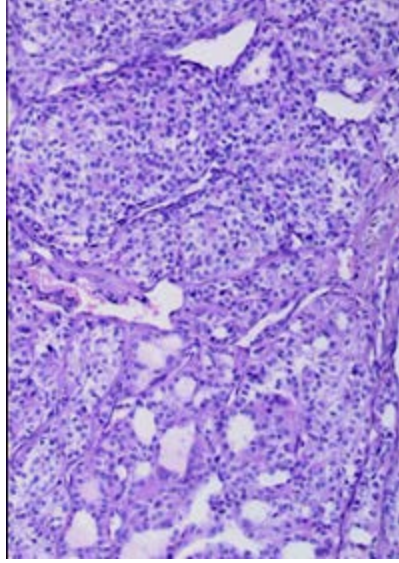
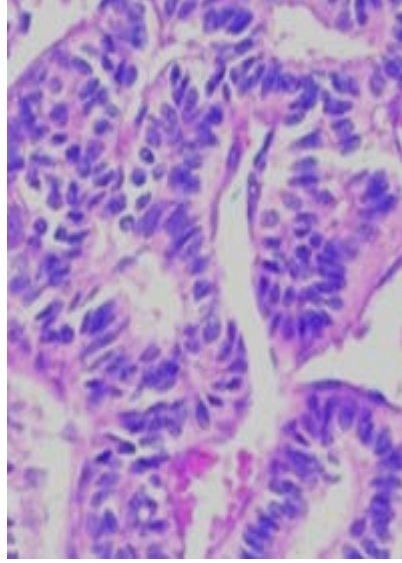
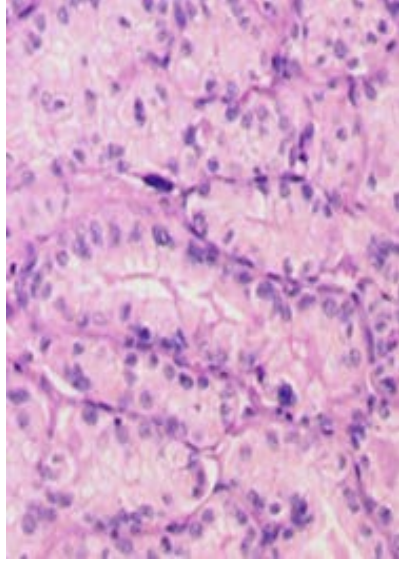
# Tiroid Nodülleri



SurePath Sitoloji	Malignite Sayısı	Morfolojik tipler
Tanısal olmayan	2	2 Klasik PTK
Benign	6	1 Medüller karsinom 2 FvPTK 3 Minimal İnvaziv Folliküler karsinom
AUS/FL-US	4	1 FvPTK 3 Minimal İnvaziv Folliküler karsinom
FN/ FN?	13	8 FolCa (6 Minimal İnvaziv Folliküler, 2 Yaygın İnvaziv Folliküler karsinom) 5 PTK (1Klasik, 4 FvPTK)
Malignite şüphesi	52	50 PTK (18'i FvPTK) 2 Medüller karsinom
Malign	169	166 PTK (25'i FvPTK) 1 Medüller karsinom 1 Az diferansiye tiroid karsinomu 1 Anjiyosarkom

Kısaltmalar: PTK:Papiller tiroid karsinomu, Fv:Folliküler varyant

# Morfolojik korelasyon



**Tiroid İnce İğne Aspirasyonu Sıvı Bazlı (*SurePath*) Sitoloji-  
Histoloji Korelasyonu  
(Bethesda II,III,IV,V,VI için)  
Test istatistikleri-1\***

•Yalancı Pozitiflik: (2/485) %0.4

1 Hashimoto tiroiditi  
1 Hıyalinize trabeküler tümör

•Yalancı Negatiflik: (6/485) %1.2

1 Medüller karsinom  
2 Folliküler varyant PTK  
3 Minimal invaziv Folliküler karsinom

\*: Benign neoplazmlar hariç

Tiroid İnce İğne Aspirasyonu Sıvı Bazlı ( <i>SurePath</i> ) Sitoloji-Histoloji Korelasyonu (Bethesda II,III,IV,V,VI için) (Test istatistikleri-2*)		Oranlar**
Duyarlılık (Sensitivite)	%96.6	%43-100
Özgüllük (Spesifite)	%82	%52-100
Pozitif Prediktif Değer (PPV)	%92.3	%34-100
Negatif Prediktif Değer (NPV)	%91.5	%83-99
Doğruluk ( <i>Accuracy</i> )(+) <i>LR</i> ( <i>Olabilirlik oranı:Likelihood Ratio</i> ) (10 üzeri tanıyı doğrulamak için güçlü kanıt) (-) <i>LR</i> (0.1 altı tanıyı dışlamak için güçlü kanıt)	%92 5.39 (orta-iyi) 0.04	%75-100  **Demay, <i>The Arts &amp; Science of Cytopathology</i> , sf. 852
*: Benign Neoplazmlar dahil		

# Sonuç ve Tartışma

## Sıvı Bazlı (SurePath) Sitoloji;

- Tek başına alternatif sitolojik yöntemdir.
- Sensitivitesi yüksek, spesifitesi benzer; Tanısal doğruluğu yüksektir.
- Paterni ve sitomorfolojik özellikleri korur.
- Kromatinin boyanması (hipokrom/hiperkrom ayrımı) netlik kazanır.
- Sitoplazma, kolloid ve zemin materyalleri boyanır.
- Tarama ve inceleme zamanını kısaltır; tek lamda hücreleri toplar.
- Sadece 'Kist içeriği makrofajlar' olan (tanısal olmayan grubun %10'una yakın) materyallerin değerlendirmesini kolaylaştırır.
- Hücre bloğu ve immünohistokimya yapılabilir.
- Özgüllüğü etkileyen ara lezyonlarda DNA mutasyon analizleri yapılabilir.
- On-site (yerinde) TiiAS yapılamayan yerlerde öncelikle tercih edilebilir.
- 2-3 ay Konvansiyonel (Pap/MGG) birlikte kullanım sonrası tümüyle Sıvı Bazlı sisteme geçilebilir.

