

Kanser Tanı ve Tedavisinde Bilgisayar Destekli Mikroskopi

Dijital Patoloji

Rengül Çetin-Atalay, MD PhD

Kanser Sistem Biyolojisi Laboratuvarı

Enformatik Enstitüsü

Sağlık Bilişimi Bölümü

Orta Doğu Teknik Üniversitesi

KANSER

Kanser dokulardaki normal hücrelerin düzensiz olarak bölünüp çoğalmasıyla beliren yayılımcı kötü urlara denir.

Dünya Sağlık Örgütü verilerine göre kanser hastalık olgularında ve ölümlerinde önde gelen bir hastalığıdır. Her yıl 14 milyon yeni olgu rapor edilmektedir.

2030 yılında kanser kaynaklı ölümlerin 13.1 milyona ulaşması beklenmektedir.

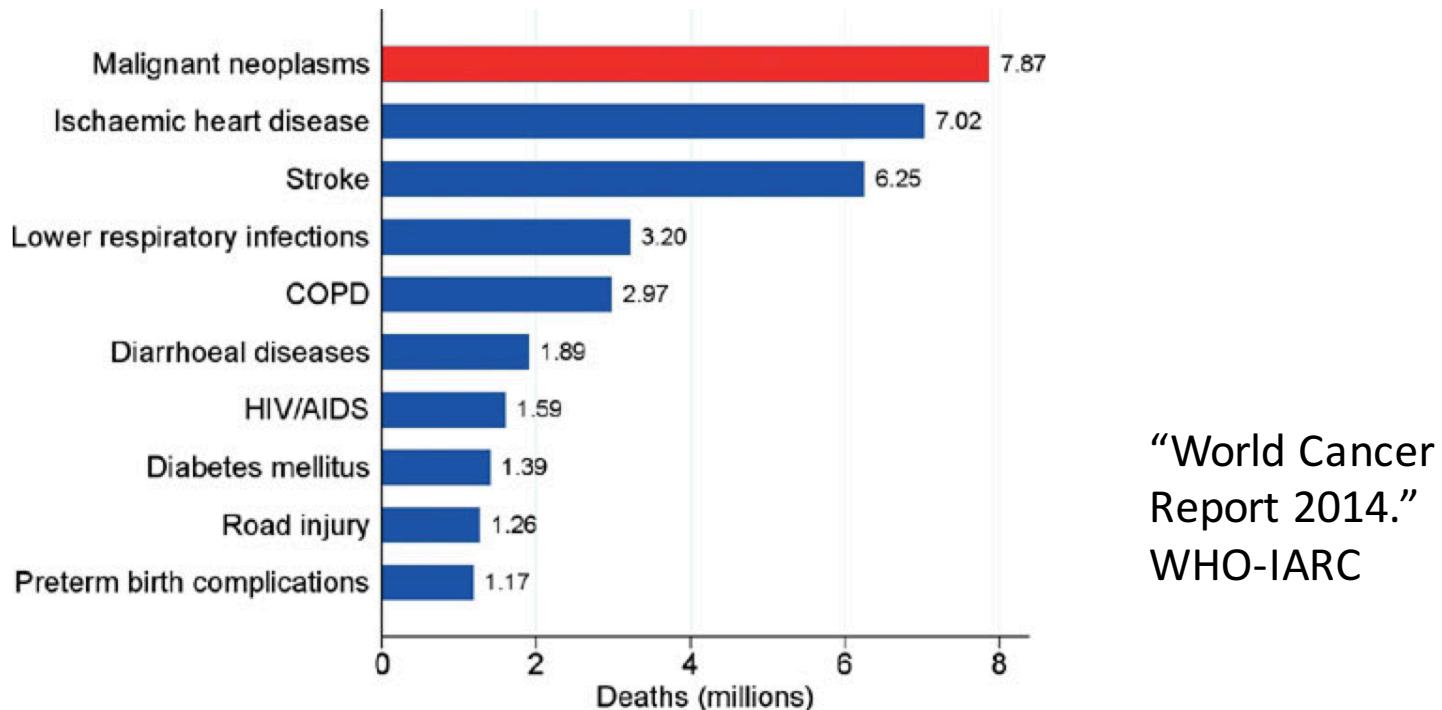
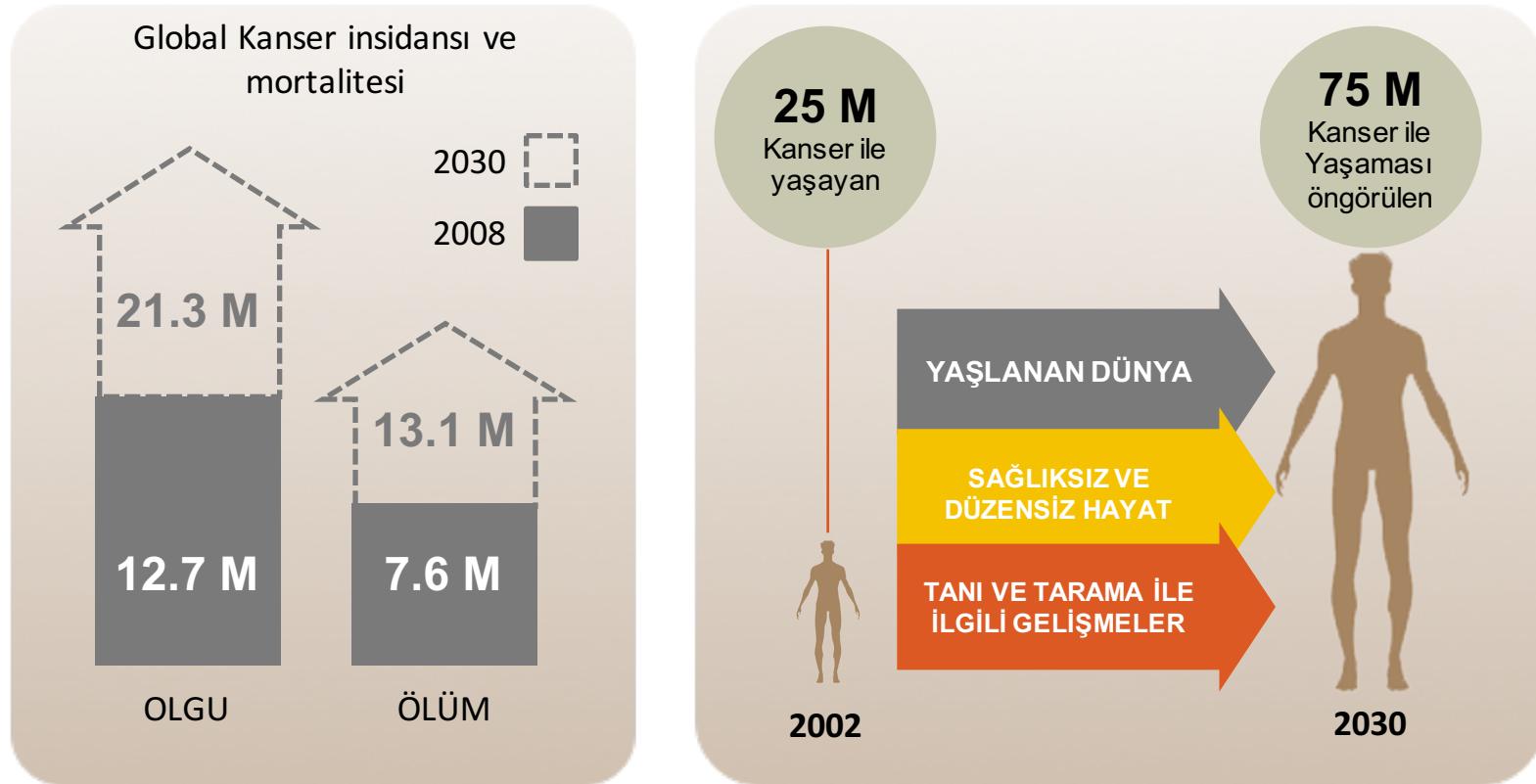


Fig. 1.2.2. The 10 leading causes of death worldwide in 2011. COPD, chronic obstructive pulmonary disease.

Kanser yoğunluğu



The International Agency for Research on Cancer. *World Cancer Report 2008*

<http://globocan.iarc.fr>

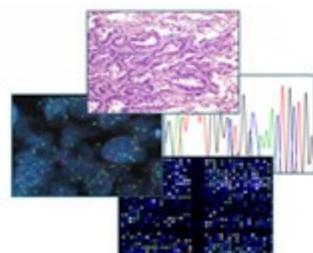
http://w2.iarc.fr/en/publications/pdfs-online/wcr/2008/wcr_2008.pdf

korunma, erken tanı ve tedavi

Kişiye özgü kanser tanı ve tedavisi



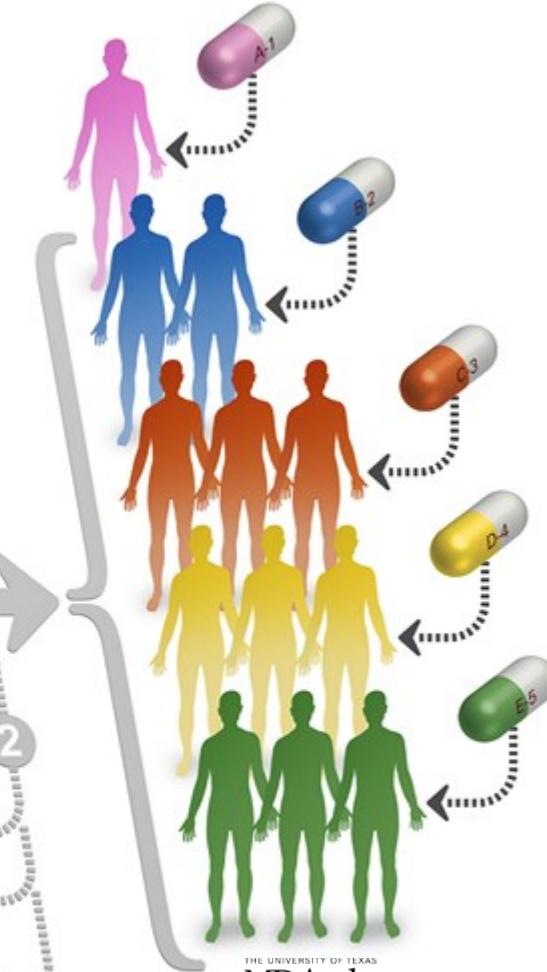
Moleküler profil



Öngörü belirteçleri

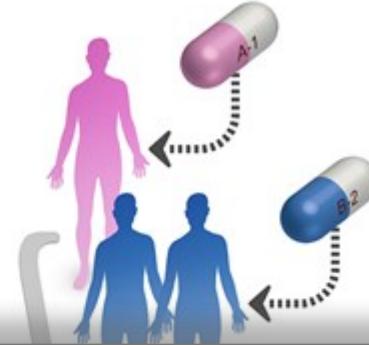
Ayırıcı tanı

İlaç tedavisine yanıt



THE UNIVERSITY OF TEXAS
MD Anderson
~~Cancer~~ Center
Making Cancer History®

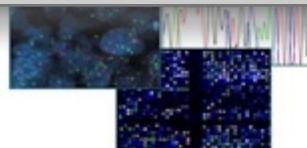
Kişiye özgü kanser tanı ve tedavisi



Doğru tanı ve tedavi

- Bütünleştirilmiş moleküller genetik, **dijital patoloji** ve **genomik patoloji**
- Hekimler hastalarına özgü ve uygun tedavi planını planlayabilirler.

Dr. David Roth, Director of the Precision Medicine Program at Penn



İlaç tedavisine yanıt

MDAnderson
Cancer Center
Making Cancer History®

Meme kanseri tanı ve tedavisi

Klinik şikayet

Meme kanseri tanı ve tedavisi

Mammografi

Klinik şikayet



<http://images.medicinenet.com/images/slideshow/breast-cancer-s8-photo-of-breast-biopsy.jpg>

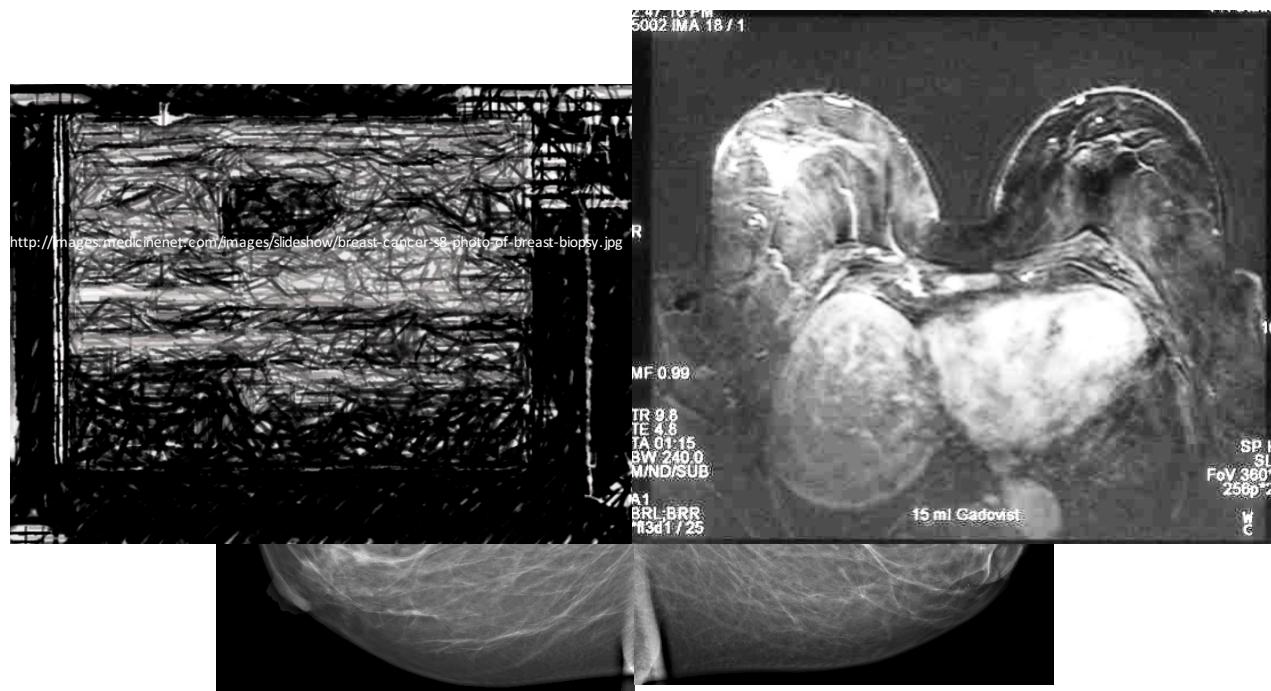
Meme kanseri tanı ve tedavisi

MRI

Mamma Sonografi

Mammografi

Klinik şikayet



http://images.medicinenet.com/images/slideshow/breast-cancer-s8-photo-of-breast-biopsy.jpg

Meme kanseri tanı ve tedavisi

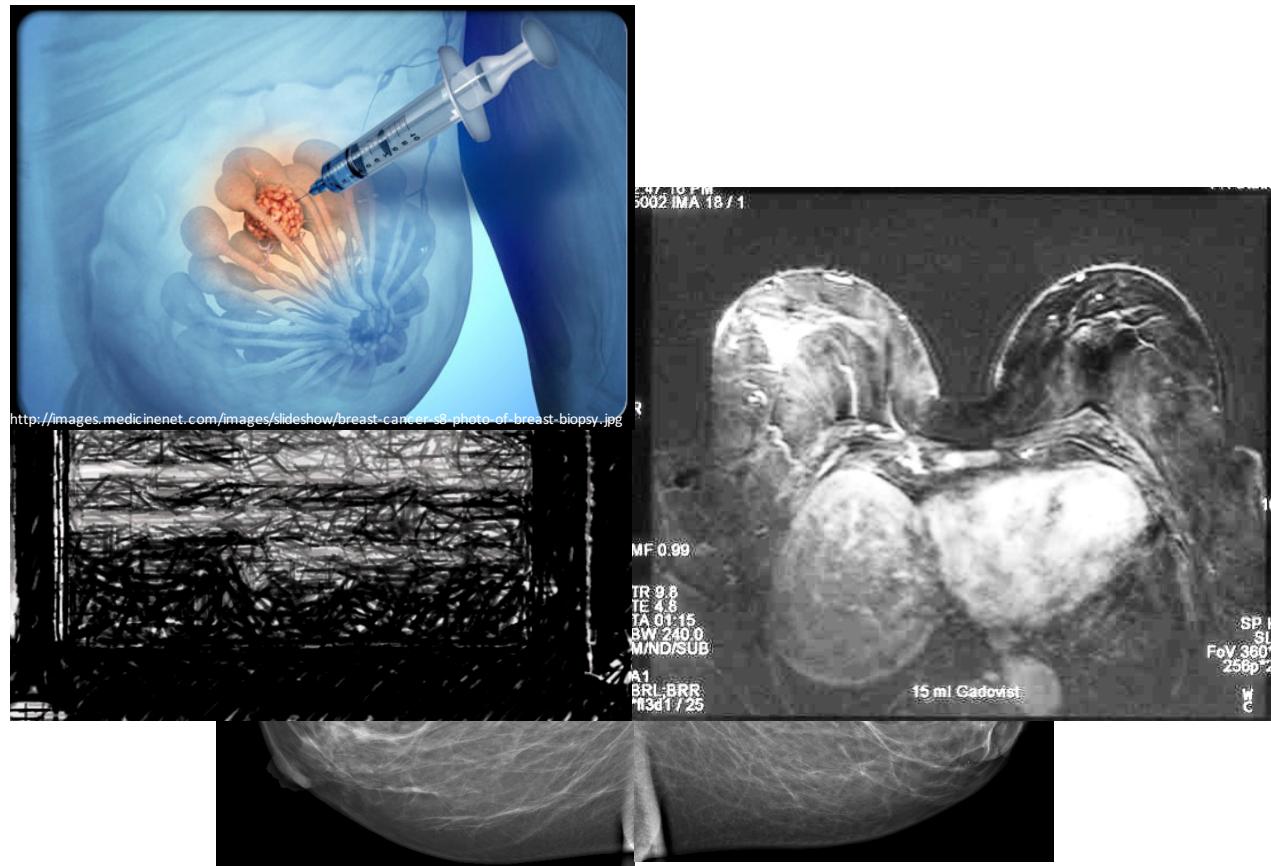
Görüntü destekli örnek

MRI

Mamma Sonografi

Mammografi

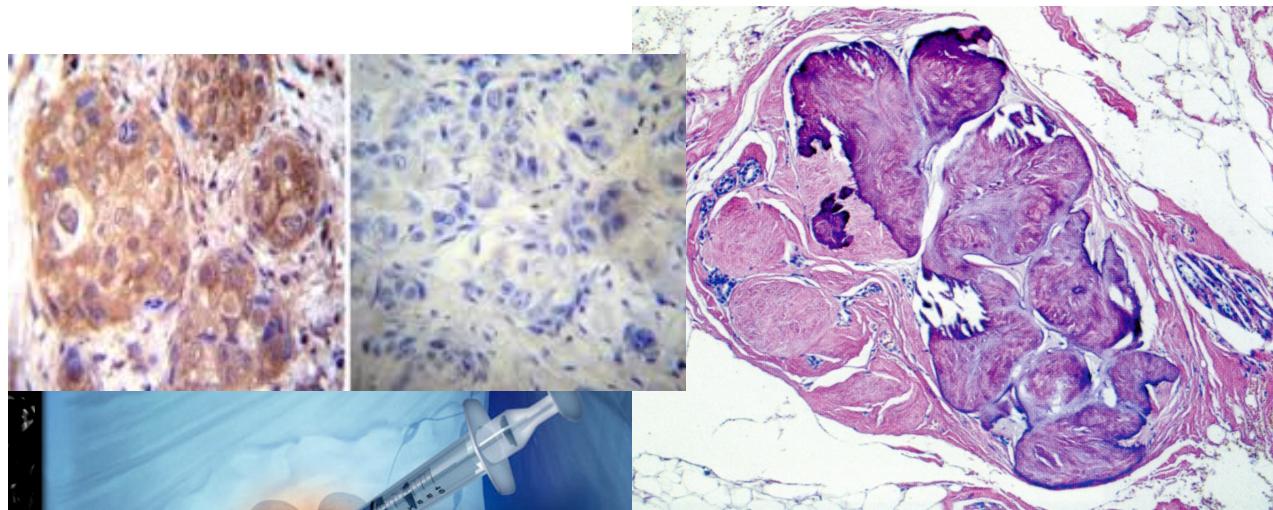
Klinik şikayet



<http://images.medicinenet.com/images/slideshow/breast-cancer-s8-photo-of-breast-biopsy.jpg>

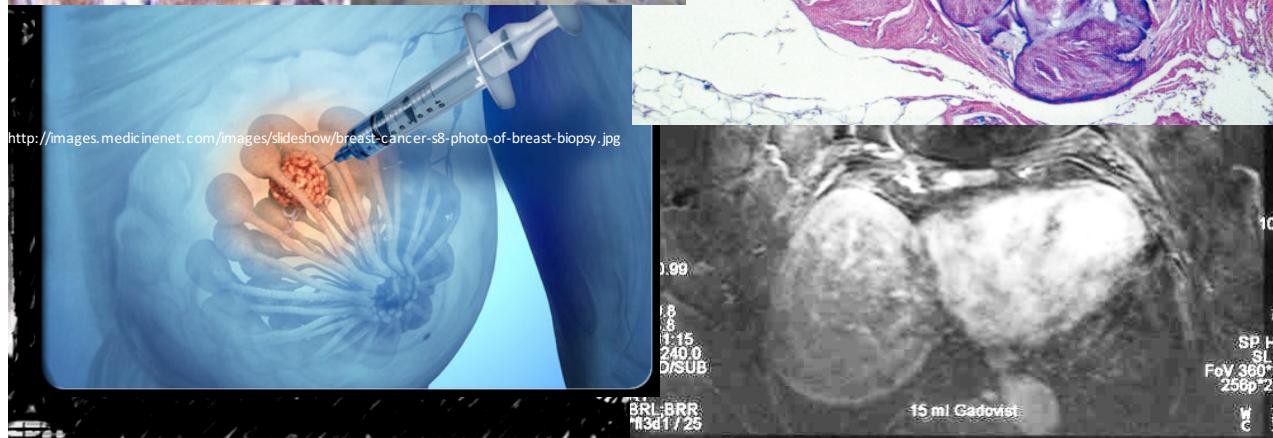
Meme kanseri tanı ve tedavisi

Patoloji



Görüntü destekli örnek

MRI



Mamma Sonografi

Mammografi

Klinik şikayet



<http://images.medicinenet.com/images/slideshow/breast-cancer-s8-photo-of-breast-biopsy.jpg>

Meme kanseri tanı ve tedavisi

Tümör kurulu

Patoloji

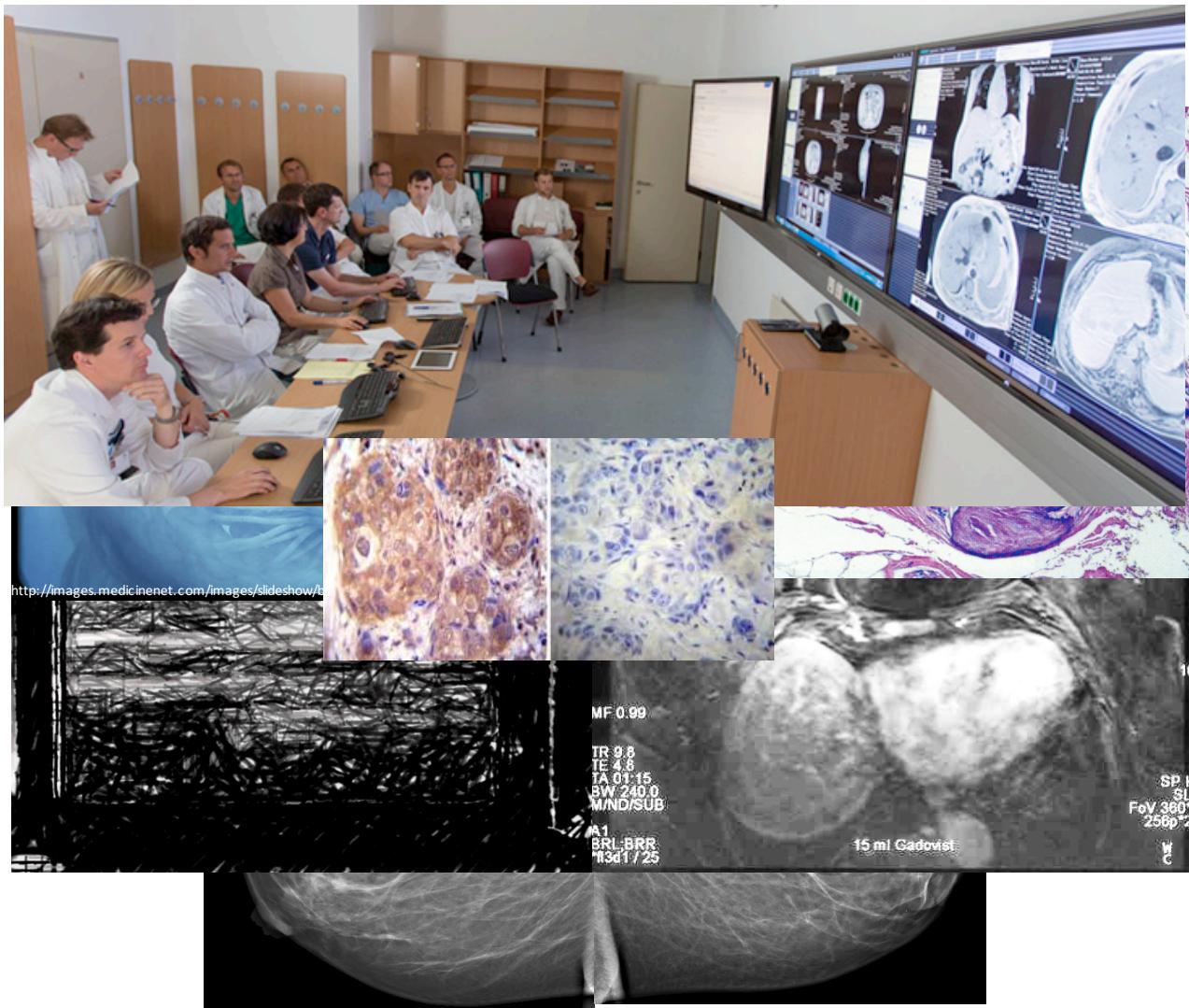
Görüntü destekli örnek

MRI

Mamma Sonografi

Mammografi

Klinik şikayet



<http://images.medicinenet.com/images/slideshow/breast-cancer-s8-photo-of-breast-biopsy.jpg>

Meme kanseri tanı ve tedavisi

Tedavi

Tümör kurulu

Patoloji

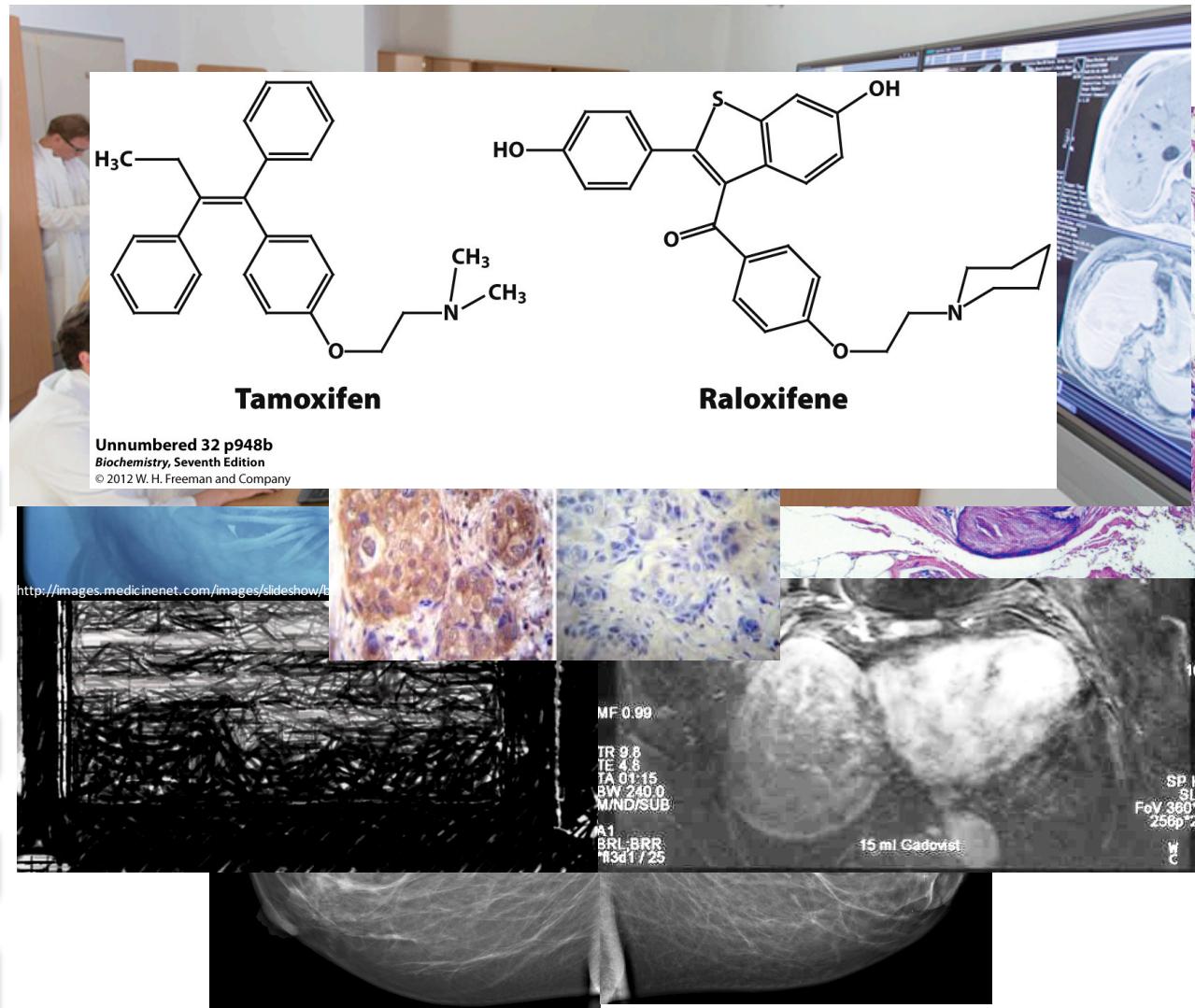
Görüntü destekli örnek

MRI

Mamma Sonografi

Mammografi

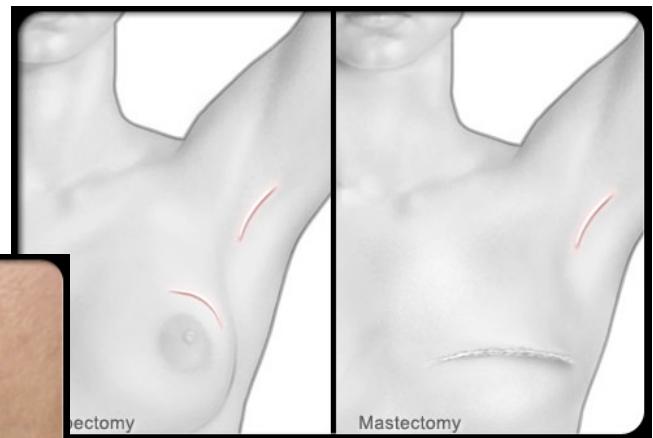
Klinik şikayet



.... Kişiye özgü tedavi



Cerrahi



Hormon



Kemo

Radyasyon

Bilgisayar destekli mikroskopi

Sınıflama

karakterizasyon

Bölütleme

Saklama ve Taşıma

Dijital birleştirme

doku taranması

İşaretleme ve tanımlama

Klinik doku örneği

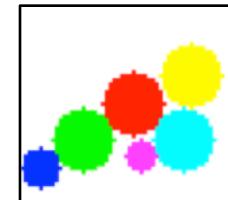
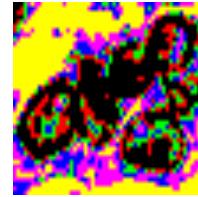
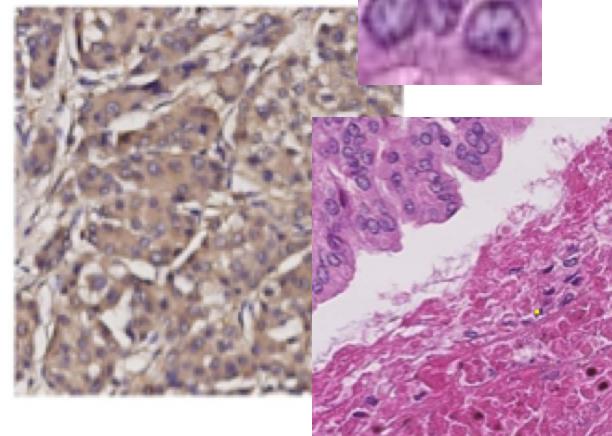
Yazılım (Software)



Donanım (Hardware)



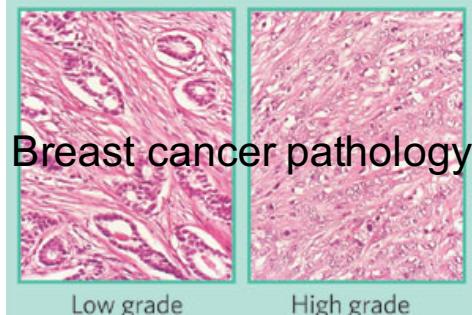
Laboratuvar (Wetware)



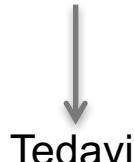
Ayrımsal tanı dijital patoloji



Traditional clinical pathology
H&E



Derecelendirme (grading)

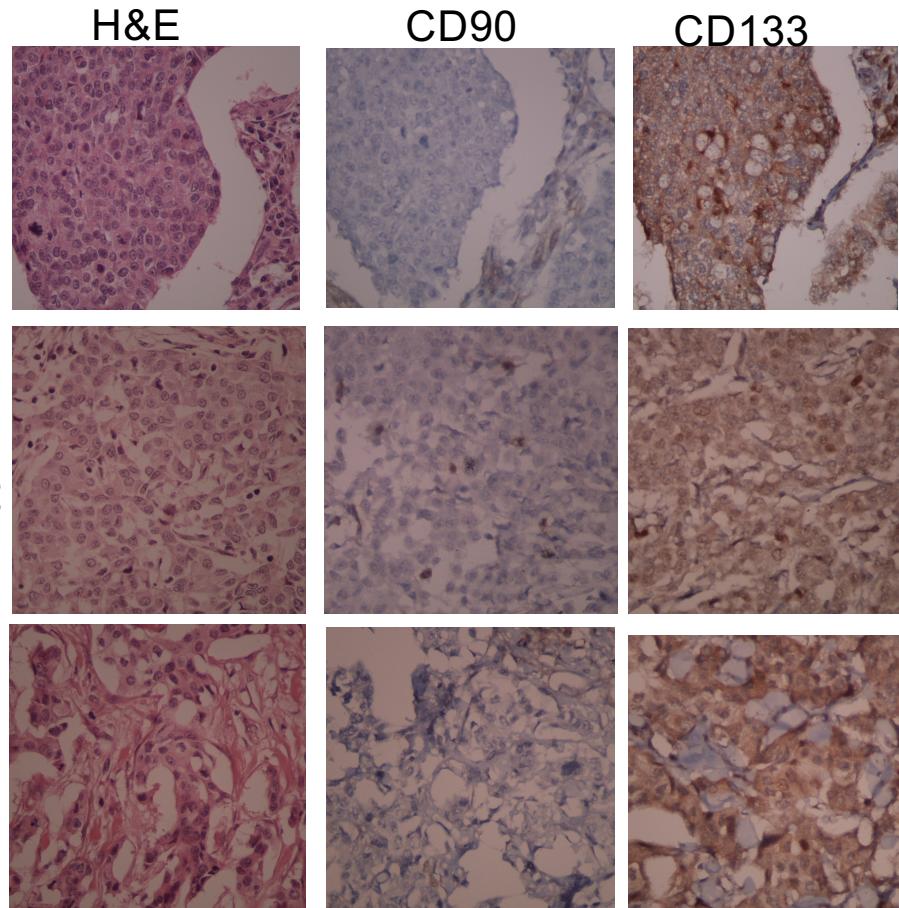


Tedavi

Enabling personalized cancer medicine through analysis of gene-expression patterns Laura J. van 't Veer & René Bernards
Nature 452, 564-570

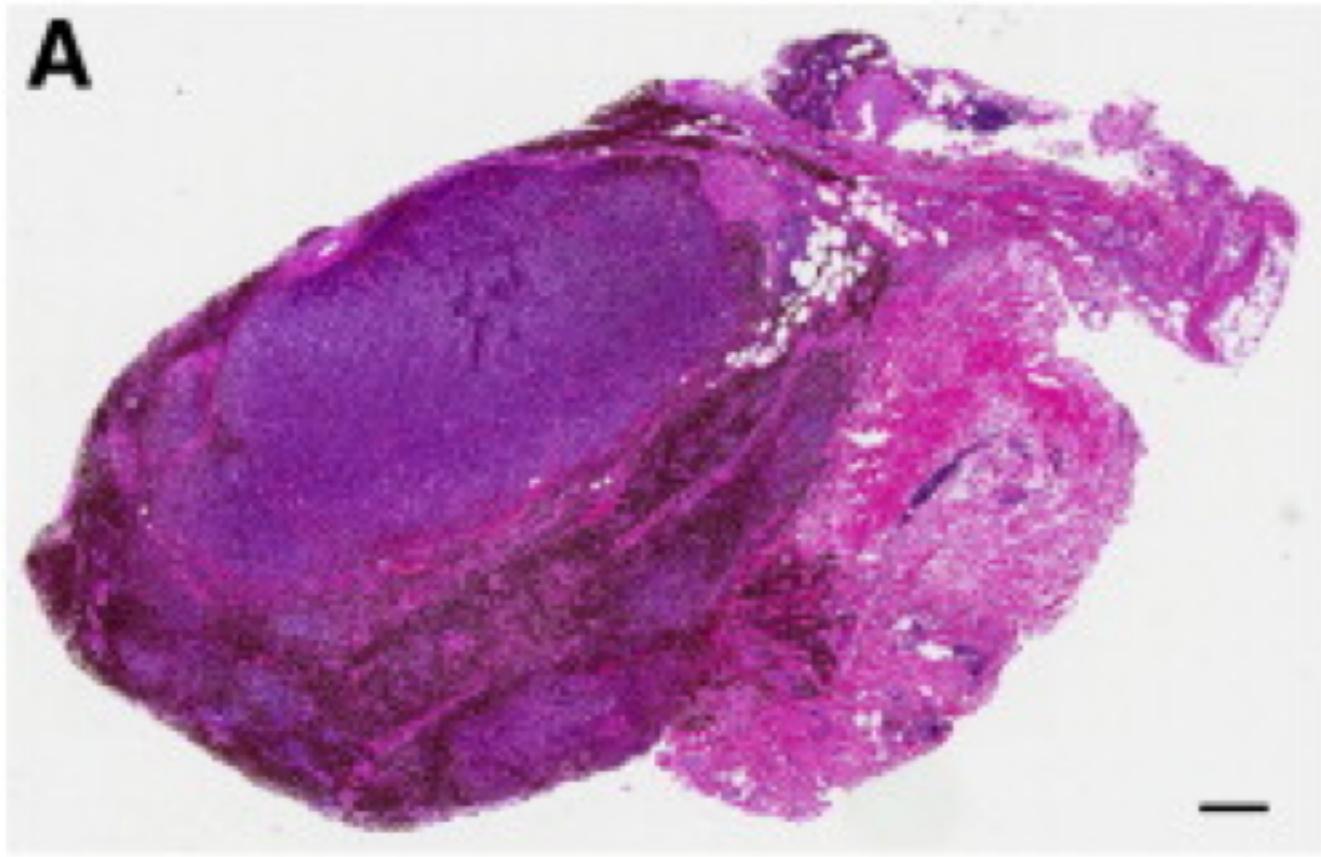
İleri seviye Meme kanseri hasta örnekleri

Automated microscope with molecular cancer stem cell markers (CD90 and CD133)



Atalay Lab örnekleri

KanSiL



Bih-Rong Wei, R. Mark Simpson

Digital pathology and image analysis augment biospecimen annotation and biobank quality assurance harmonization

Clinical Biochemistry, Volume 47, Issues 4–5, 2014, 274–279

<http://dx.doi.org/10.1016/j.clinbiochem.2013.12.008>

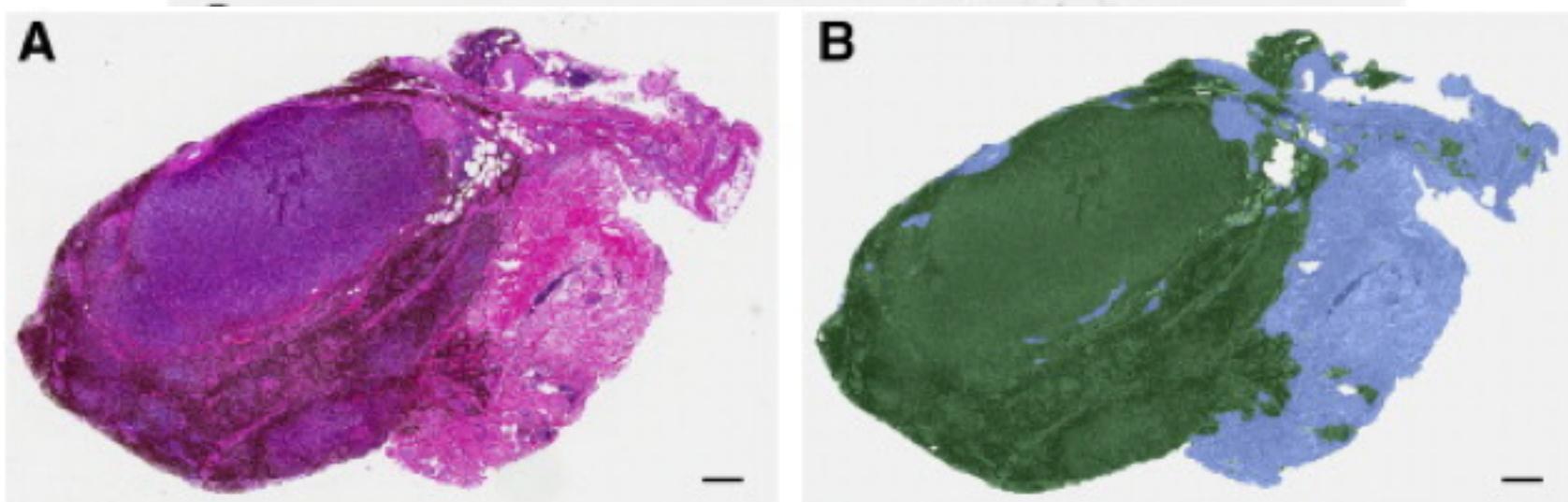


Fig. 1. Automated pattern recognition image analysis approach for quantifying tissue features in biobank tissue specimens as part of pathology quality assurance. Unique algorithms were developed for each tumor type. A. Sub-gross photomicrograph of an optically scanned melanoma tissue section image used for morphometric analysis is displayed as a representative example. Hematoxylin and eosin stain. B. Tissue section shown in (A) after image analysis, displayed with pseudo-color mark-up revealing tissue areas segmented as cancer (green, 68.6%) and stroma (blue, 31.4%).

Bih-Rong Wei, R. Mark Simpson

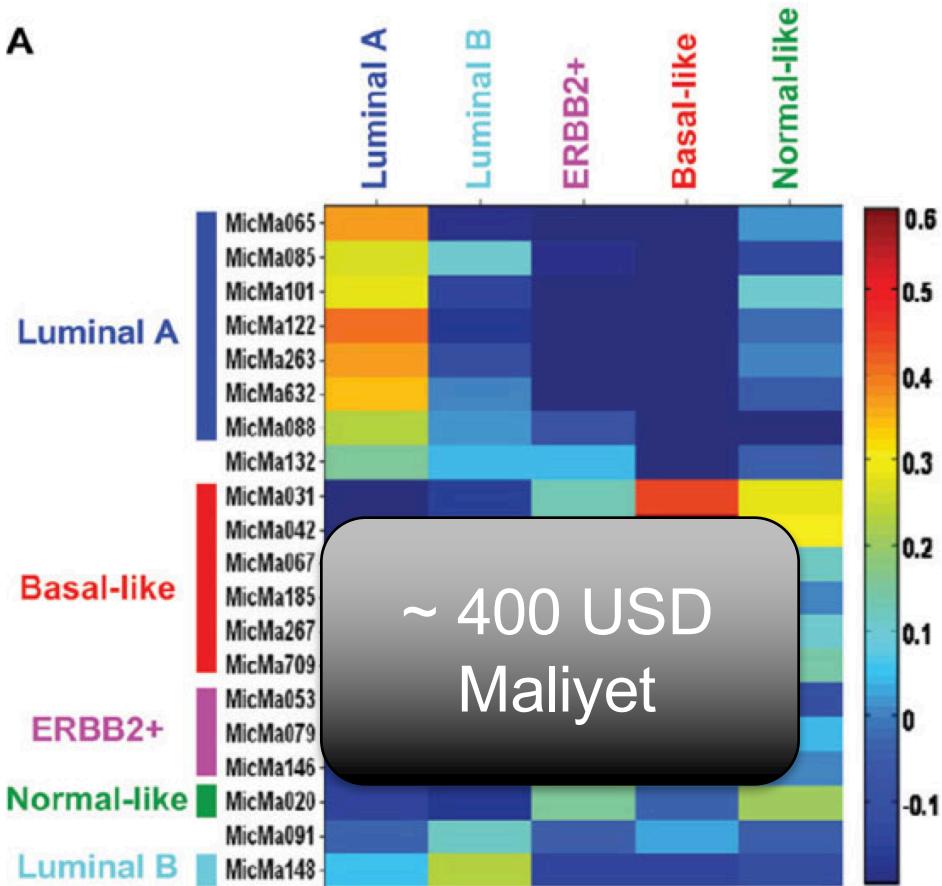
Digital pathology and image analysis augment biospecimen annotation and biobank quality assurance harmonization

Clinical Biochemistry, Volume 47, Issues 4–5, 2014, 274–279

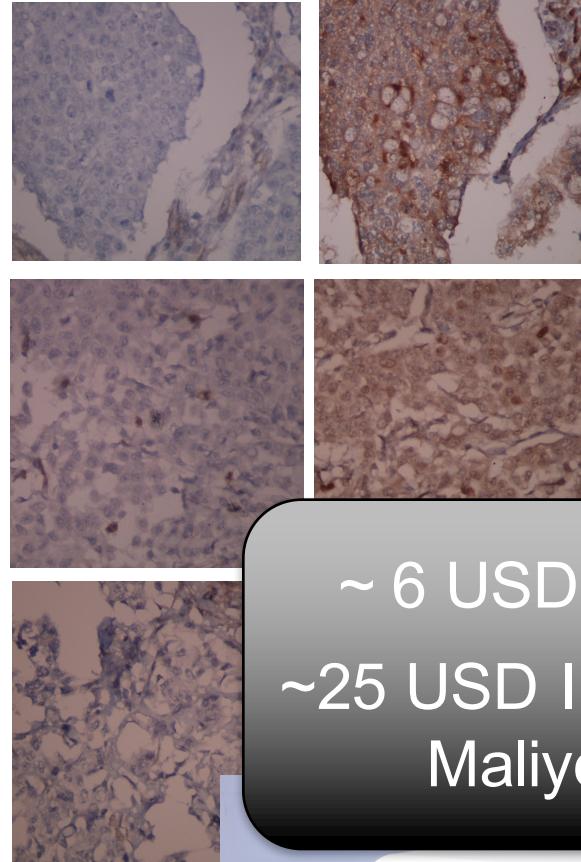
<http://dx.doi.org/10.1016/j.clinbiochem.2013.12.008>

Kişiye özgü tanı

A



Kişiye özgü moleküler analiz

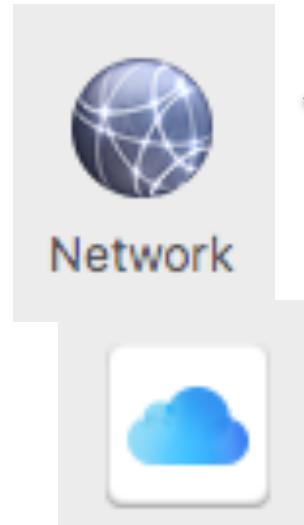


Kişiye özgü patolojik analiz

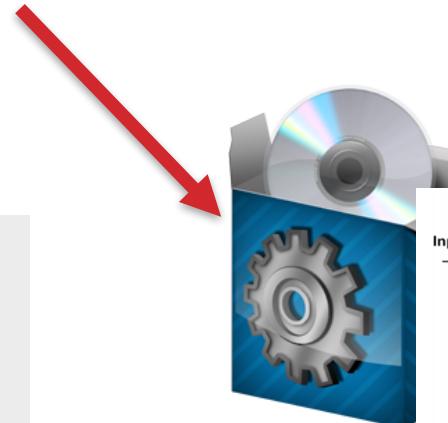


Telepatoloji

Sağlık merkezi veya
ameliyathane



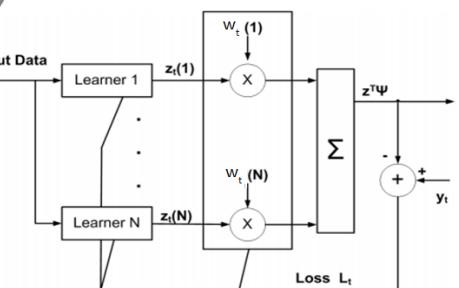
Network



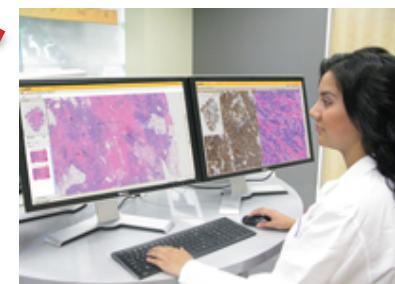
tanı

Merkezi Hastane
Patoloji Bölümü

Dijital patolojik tanı

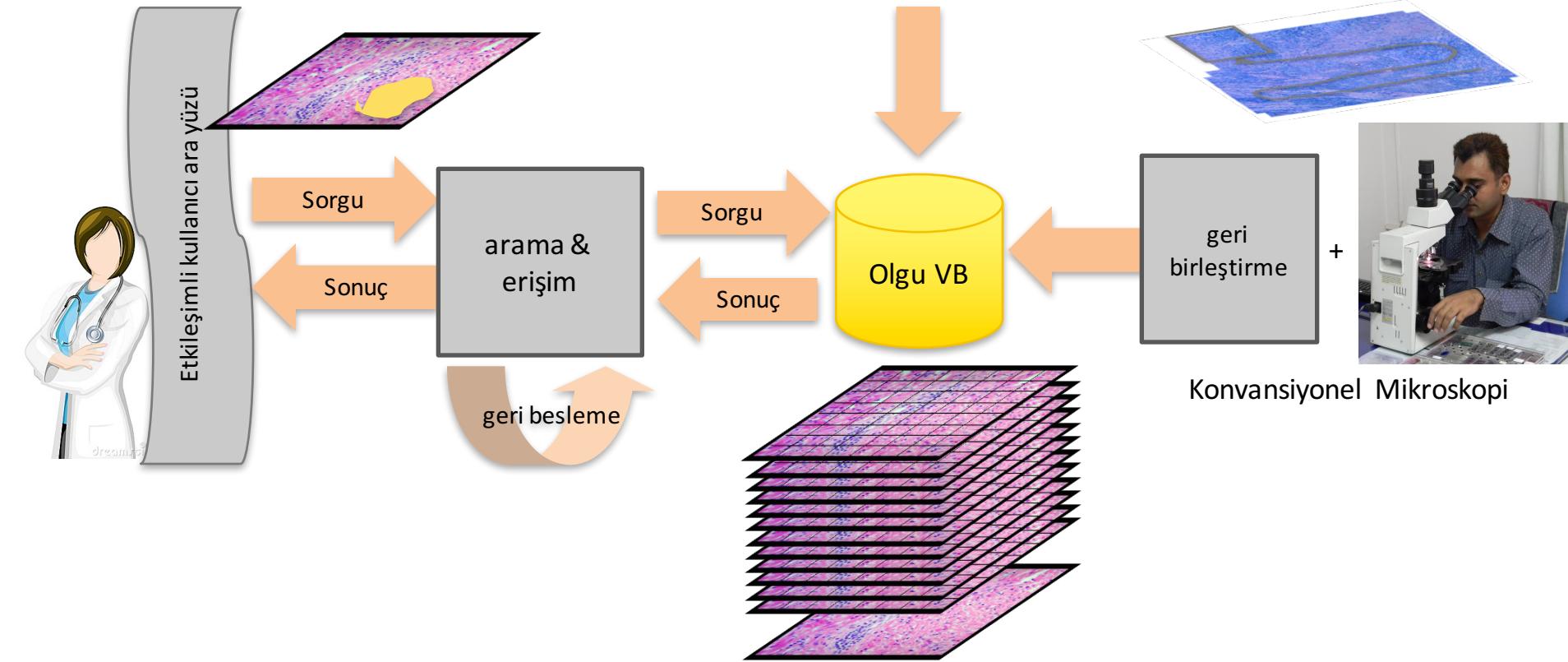


Dijital tanının
Doğrulanması

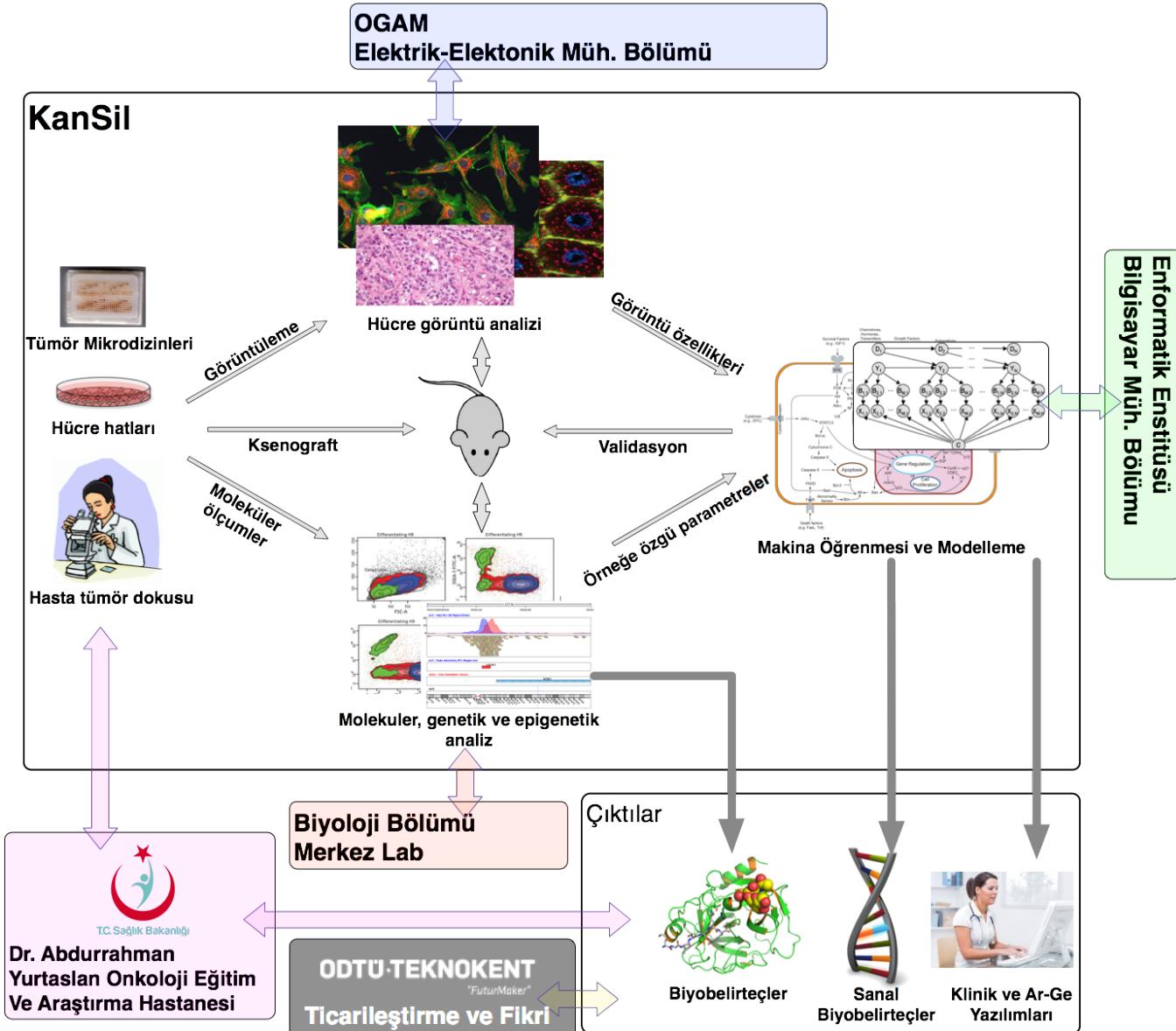




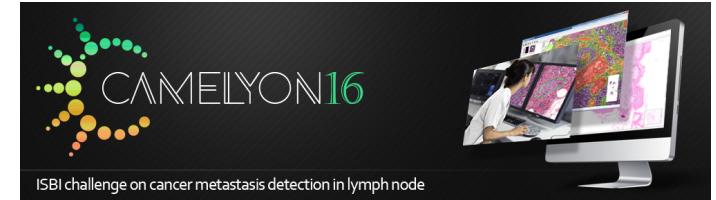
Dijital cam tarayıcı



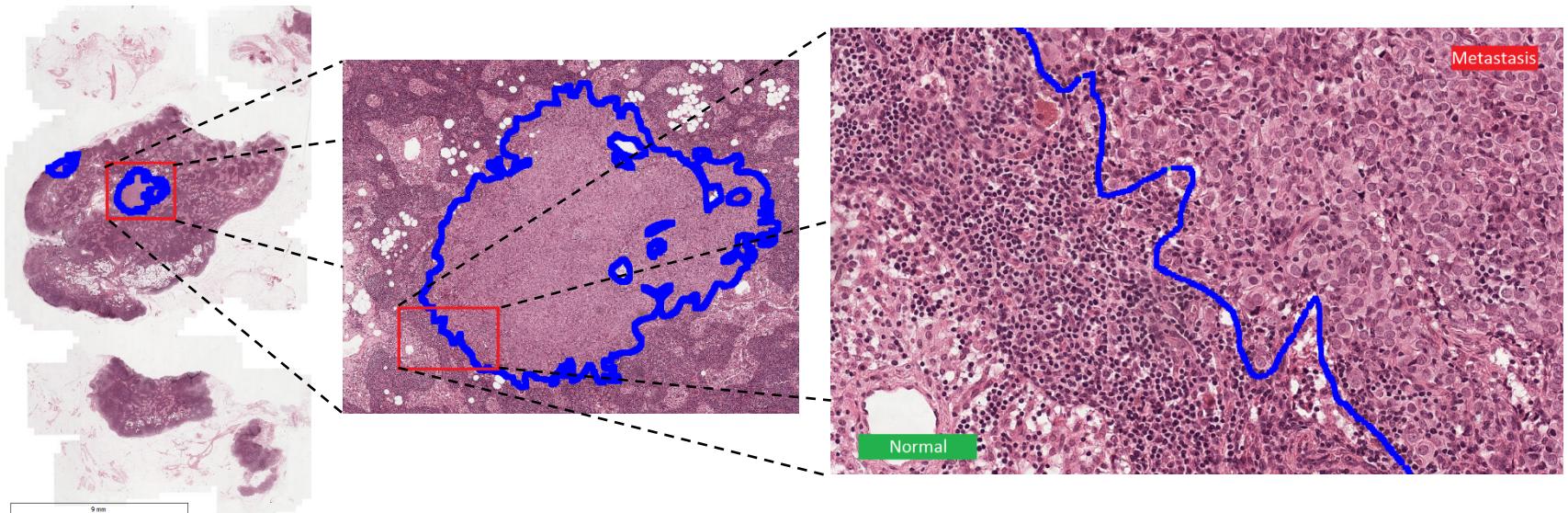
KanSil Araştırma Yapısı



Sentinel lymph node biopsy (SLNB)



- Amacı H&E boyalı meme kanseri sentinel lenf nodları dokularında metastatik bölgelerin otomatik olarak bulunması
- ISBI (International Symposium on Biomedical Imaging) tüm digital cam histopatoloji görüntü analizi



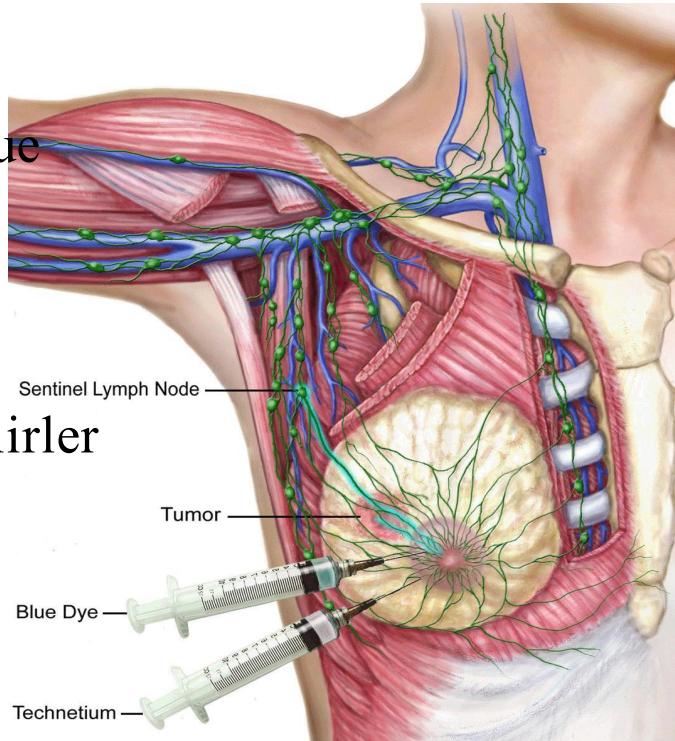
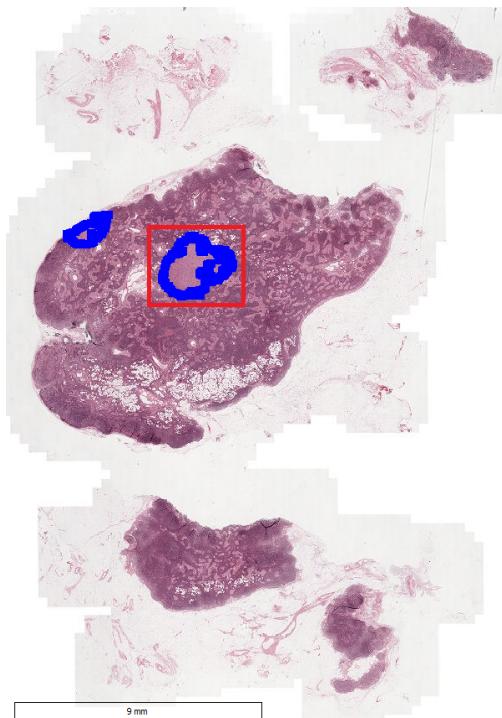
20 Gigapixel images

Sentinel Lenf Nodu

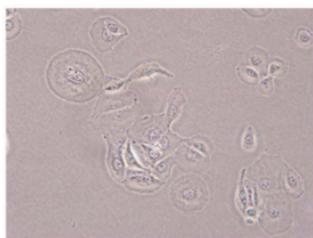
- Teknisiyum işaretli sülfür kolloid ve Isosulfan blue (lymphazurin 1%)

■ Lenf nodu patolojisi

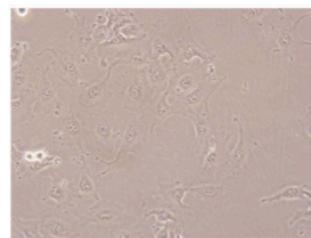
- Kanserin yayılma potansiyelini (metastaz) belirler



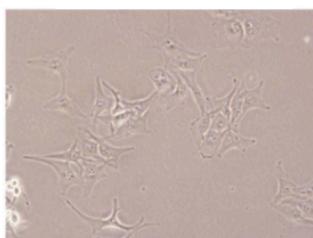
Kanser Hücre hattı sınıflaması



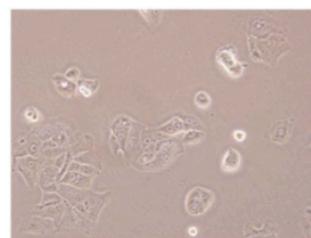
BT-20-Breast



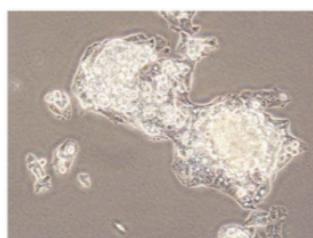
Mahlavi-Liver



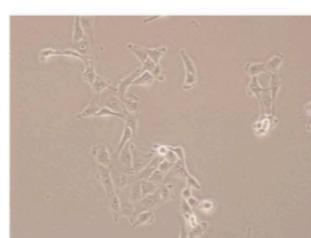
FOCUS-Liver



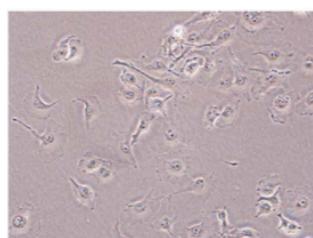
PLC-Liver



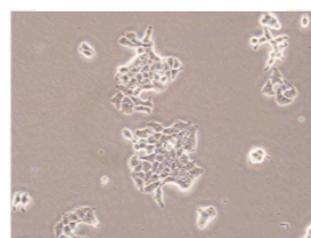
Hep-G2-Liver



SkHep-1-Liver



MDA-MB-157-Breast



T47D-Breast

OPEN ACCESS Freely available online

PLOS ONE

Image Classification of Human Carcinoma Cells Using Complex Wavelet-Based Covariance Descriptors

Furkan Keskin¹, Alexander Suhre¹, Kivanc Kose¹, Tulin Ersahin², A. Enis Cetin¹, Rengul Cetin-Atalay^{2*}

¹ Electrical and Electronics Engineering Department, Bilkent University, Ankara, Turkey, ² Department of Molecular Biology and Genetics, Bilkent University, Ankara, Turkey

Abstract

Cancer cell lines are widely used for research purposes in laboratories all over the world. Computer-assisted classification of cancer cells can alleviate the burden of manual labeling and help cancer research. In this paper, we present a novel computerized method for cancer cell line image classification. The aim is to automatically classify 14 different classes of cell lines including 7 classes of breast and 7 classes of liver cancer cells. Microscopic images containing irregular carcinoma cell patterns are represented by subwindows which correspond to foreground pixels. For each subwindow, a covariance descriptor utilizing the dual-tree complex wavelet transform (DT-CWT) coefficients and several morphological attributes are computed. Directionally selective DT-CWT feature parameters are preferred primarily because of their ability to characterize edges at multiple orientations which is the characteristic feature of carcinoma cell line images. A Support Vector Machine (SVM) classifier with radial basis function (RBF) kernel is employed for final classification. Over a dataset of 840 images, we achieve an accuracy above 98%, which outperforms the classical covariance-based methods. The proposed system can be used as a reliable decision maker for laboratory studies. Our tool provides an automated, time- and cost-efficient analysis of cancer cell morphology to classify different cancer cell lines using image-processing techniques, which can be used as an alternative to the costly short tandem repeat (STR) analysis. The data set used in this manuscript is available as supplementary material through <http://signal.ee.bilkent.edu.tr/cancerCellLineClassificationSampleImages.html>.

Keskin et al, PlosOne, 2014

Smart Markers for Watershed-Based Cell Segmentation

Can Fahrettin Koyuncu¹, Salim Arslan¹, Irem Durmaz², Rengul Cetin-Atalay², Cigdem Gunduz-Demir^{1*}

1 Department of Computer Engineering, Bilkent University, Ankara, Turkey, **2** Department of Molecular Biology and Genetics, Bilkent University, Ankara, Turkey

Abstract

Automated cell imaging systems facilitate fast and reliable analysis of biological events at the cellular level. In these systems, the first step is usually cell segmentation that greatly affects the success of the subsequent system steps. On the other hand, similar to other image segmentation problems, cell segmentation is an ill-posed problem that typically necessitates the use of domain-specific knowledge to obtain good results. In this work, we propose a new approach to incorporate this knowledge into their segmentation process. We introduce three types of smart markers to segment the cells. The proposed approach is evaluated on the test set and compared with the state-of-the-art methods.

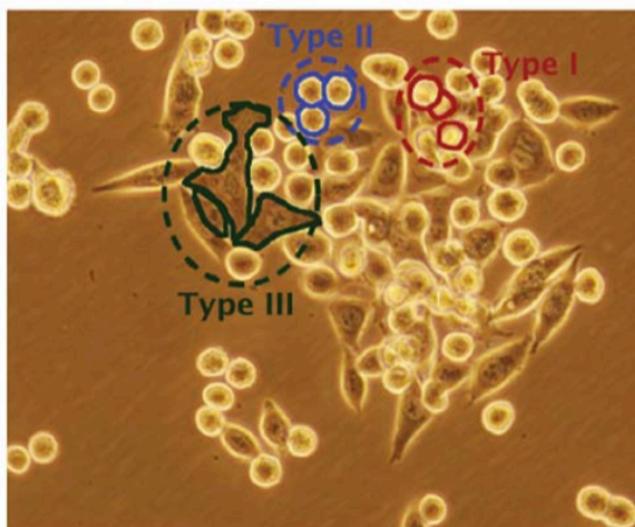


Figure 1. Example images of live KATO-3 cells. The figure shows three different morphological classes based on their visual characteristics. doi:10.1371/journal.pone.0048664.g001

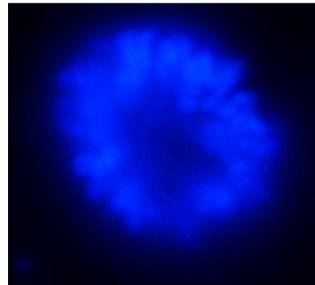
Table 4. Comparison of the marker-controlled watersheds that use the smart markers and those identified by the comparison algorithms.

	Area-based			Cell-based		
	Precision	Recall	F-score	Precision	Recall	F-score
Smart markers	0.80	0.72	0.76	0.84	0.83	0.84
Intensity-based	0.82	0.66	0.73	0.84	0.74	0.78
Distance-based	0.59	0.47	0.52	0.68	0.50	0.58
Cond-erosion	0.58	0.44	0.50	0.61	0.47	0.53

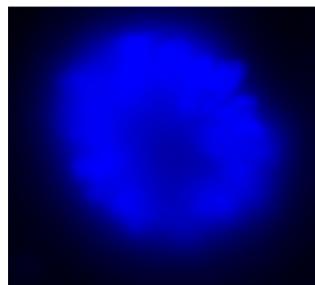
The results are obtained on the test set.
doi:10.1371/journal.pone.0048664.t004

Phase and TV Based Convex Sets for Blind Deconvolution of Microscopic Images

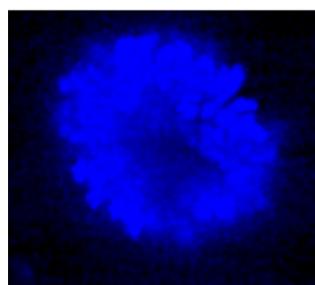
Mohammad Tofighi¹, Onur Yorulmaz¹, Kivanç Köse², Deniz Cansen Yıldırım³, Rengül Çetin-Atalay⁴, and A. Enis Çetin, *Fellow, IEEE¹*



(a)

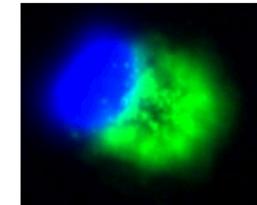


(b)

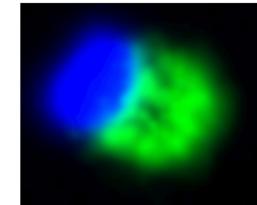


(c)

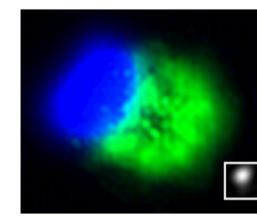
f Electrical and Electronics Engineering, Bilker
y Service, Memorial Sloan Kettering Cancer Ce
t of Molecular Biology and Genetics, Bilkent U
ent, Graduate School of Informatics, Middle Ea



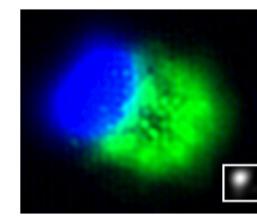
(d)



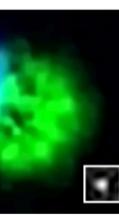
(e)



(f)



(g)

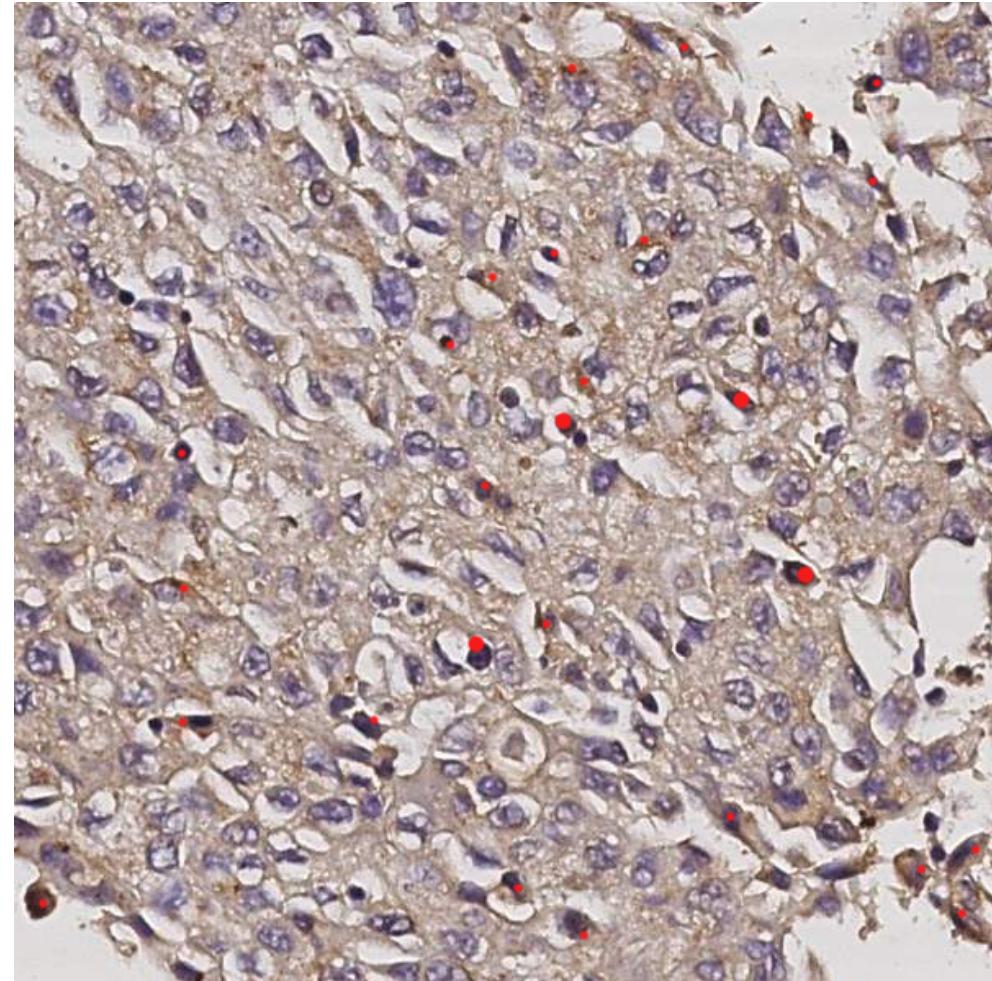
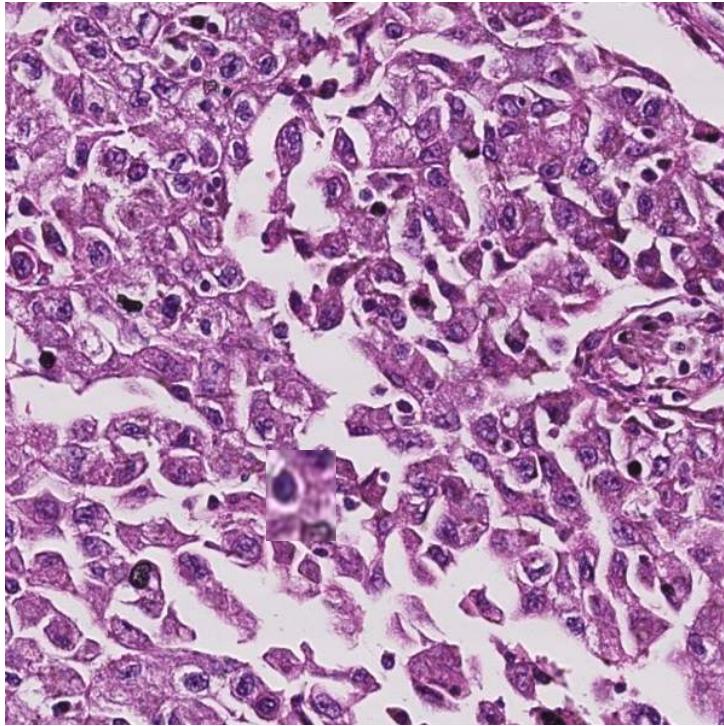


(h)

Netleştirmeye

Fig. 10: Sample deblurring results for "im-7": (a) Original image, (b) blurred image (Gaussian $\sigma = 5$); PSNR = 35.03 dB, (c) Image obtained by Ayers-Dainty with Phase and ESTV sets; PSNR = 40.24 dB, (d) Ayers-Dainty method; PSNR = 38.76 dB, (f) image obtained using [16]; PSNR = 32.32 dB. The blurring filter estimate for each case is shown in the bottom right corner.

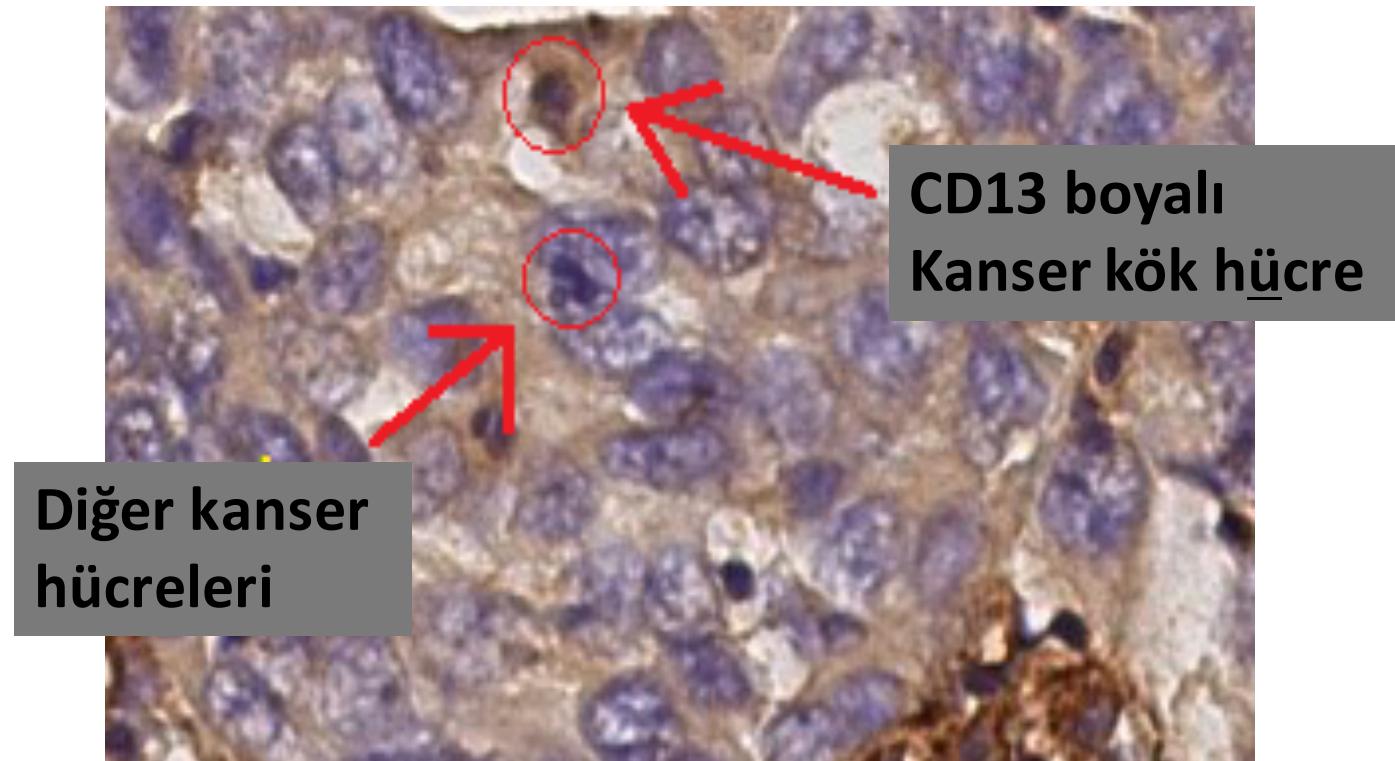
Patolojik kanser doku görüntülerinde kanser kök hücre oranının bulunması



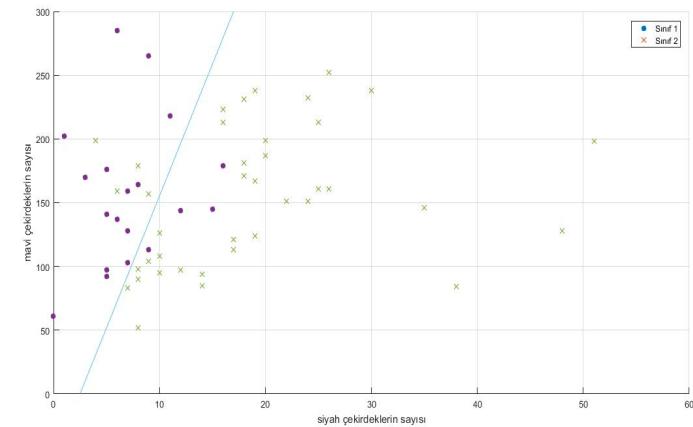
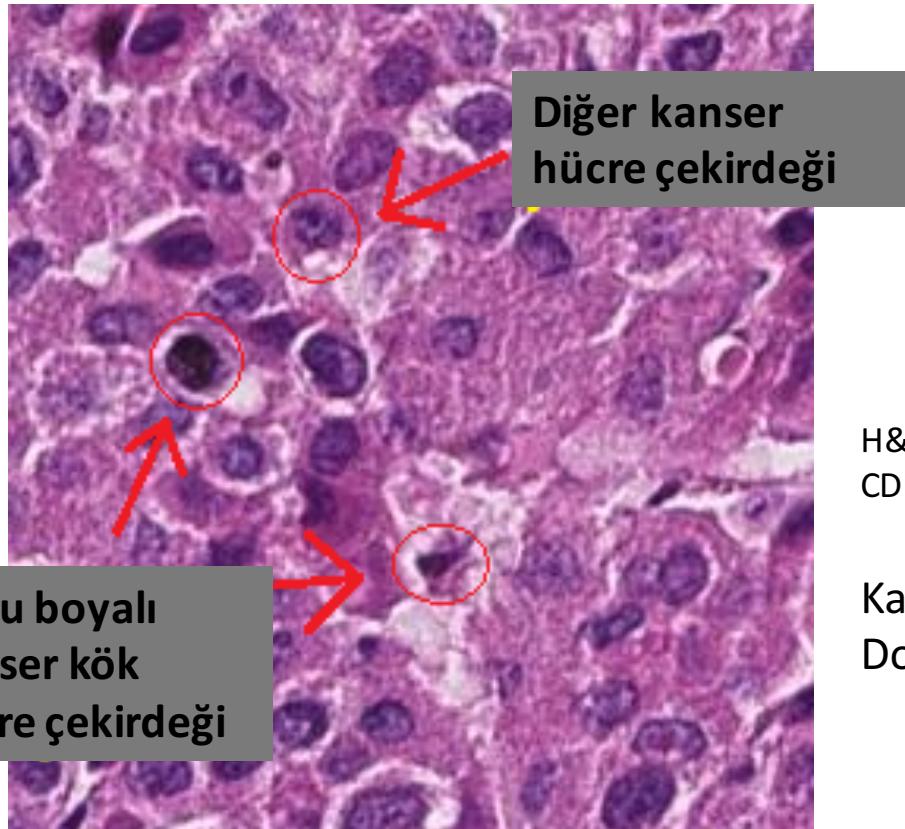
Nuclear and cellular heterogeneity

Kanser kök hücre veri seti oluşturulması

58 patoloji slaydının CD13 ile boyanmış saydamını tek tek elden geçirdik ve kahverengiye boyanmış hücre çekirdeklerini saydık.



H&E boyanmış slaytlarda bazı çekirdekler diğer çekirdeklere göre daha koyu boyanmakta ve yanlarında boşluklar oluşturmaktadır. Bu nedenle de imgelerin örüntülerinde farklılıklar oluşturmaktadır. Geliştirdiğimiz algoritma ve yazılım da bu farklılıklardan faydalananarak imgeleri sınıflandırmaktadır.



H&E ile boyanmış imgelerdeki koyu ve mavi çekirdek sayıları CD13 işaretliler ile karşılaştırılmıştır.

Kafa karıştırma (confusion) matrisi ile Doğruluk oranı %86.2 olarak hesaplanmıştır.

TEŞEKKÜRLER

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Umut Çınar

Grants

- ODTU-BAP
- TUBITAK – 1003 – 213E032
- TUBITAK – (IntenC) – LoCamSSA projesi