



ADVANCEMENTS IN LUNG CANCER TREATMENT & DIAGNOSIS

12TH ANNUAL CAYMAN ISLANDS HEALTHCARE CONFERENCE

7TH TO 9TH OCTOBER 2021

KIMPTON SEAFIRE RESORT

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OCTOBER 9, 2021



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CAUSES OF LUNG CANCER

Obvious long ago...obfuscated for decades...now PROVEN for DECADES...

Cigarettes are the leading cause of lung cancer

Some non-smokers can also get lung cancer from second hand exposure

Some occupational exposures increase lung cancer risk

'Random' DNA mutations with no clear risk factors, "...an act of God..."



Vincent Van Gogh, 1886, Art Academy of Antwerp

"...men with a history of regular cigarette smoking have a considerably higher death rate than men who have never smoked or men who have smoked only cigars or pipes..." Hammond and Horn August 7, 1954 J Am Med Assoc.

"... principal data on the death rates of smokers of various types and of nonsmokers...data from 1,123,000 men..."

U.S. Surgeon General's Report. American Cancer Society's Hammond-Horn Study and Cancer Prevention Study-I.

"...secret tobacco industry('s) propaganda...(was so effective that) as late as 1960 only one-third of all US doctors believed ...cigarettes (cause) lung cancer death... ...cigarette makers make about a penny in profit for every cigarette sold, which means that the value of a life to a cigarette maker is about US\$10 000."

Commentary, Dr Robert N Proctor, History Department, Stanford University, Stanford, California. 2013.



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SMOKING PREDISPOSES MOST CANCERS

- Lung cancer.
- Throat cancer.
- Mouth cancer.
- Nasal cavity cancer.
- Esophageal cancer.
- Stomach cancer.
- Pancreatic cancer.
- Kidney cancer.
- Bladder cancer.
- Cervical cancer.
- Acute myeloid leukemia.

<https://www.cancer.gov/about-cancer/causes-prevention/risk/tobacco/quit-smoking-pdq>



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Years of smoking finally caught up with my friend John one morning when he keeled over at work, clutching his heart. He was rushed to a hospital and peppered with questions.

"Do you smoke?" asked a paramedic.

"No," John whispered. "I quit."

"That's good. When did you quit?"

"Around 9:30 this morning."



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“Just living with a smoker increases your chance of developing lung cancer or heart disease from secondhand smoke by as much as 30 percent.”



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The Lung Health Study found that heavy smokers who received counseling from a doctor, took part in group sessions with other smokers to change their behavior, and used nicotine gum were more likely to quit smoking compared with smokers who did not receive counseling from a doctor, take part in group sessions, and use nicotine gum.

<https://www.cancer.gov/about-cancer/causes-prevention/risk/tobacco/quit-smoking-pdq>



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NICOTINE REPLACEMENT PRODUCTS

CAUTION

- Women who are pregnant or breast-feeding.
 - Teenagers.
 - People with
 - Heart rhythm problems
 - High blood pressure
 - Esophagitis
 - Ulcers
 - Insulin-dependent diabetes
 - Asthma
- Nicotine gum
 - Nicotine patches
 - Nicotine nasal spray
 - Nicotine inhalers
 - Nicotine lozenges



PHARMACEUTICALS TO QUIT SMOKING

CAUTIONS:

Aggressive behavior, anxiety, nervousness, depression and suicidal thoughts.

- Bupropion
(also called Zyban)
- Varenicline
(also called Chantix)



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The risk of lung cancer is reduced by 39.1% at 5 years after stopping smoking.

Tindle HA, Duncan MS, Greevy RA, et al. Lifetime smoking history and risk of lung cancer: results from the Framingham Heart Study. *JNCI J Natl Cancer Inst.* 2018;110(11):djy041. doi: 10.1093/jnci/djy041.



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“The long-term health effects of e-cigarettes are not fully known...an FDA study found cancer-causing substances in half the e-cigarette samples tested.”



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It's easy to quit smoking: I already did it three times!...try, try again...

“ Tomorrow we all will go to gym, start studying and working in earnest, quit smoking and drinking, will get up and go to bed early...but every day when we wake up, it's today again...”

START TODAY



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HOW BIG A PROBLEM IS LUNG CANCER IN CAYMAN ?

We don't really know...insufficient registry data

Table 1. — Average Annual Age-Adjusted* Mortality Rates for Selected Cancers (per 100,000) by Birthplace: Florida, 2008–2012

	US-Born		Born Outside the United States			
	United States All Races		Hispanic Caribbean** All Races		Majority Black Caribbean All Races	
	Deaths	Rate (95% CI)	Deaths	Rate (95% CI)	Deaths	Rate (95% CI)
Lung and Bronchus	28,023	62.3 (61.6–63.1)	2,287	44.7 (42.8–46.6)	317	21.0 (18.6–23.6)

???

“ In comparison to the total US-born Florida population, both black Caribbeans and Hispanic Caribbeans have lower all-sites-combined cancer mortality rates...”

Black Heterogeneity in Cancer Mortality: US-Blacks, Haitians, and Jamaicans. Paulo S. Pinheiro, MD et al., October 2016, Vol. 23, No. 4 Cancer Control 347



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LUNG CANCER IN MEN VS. WOMEN

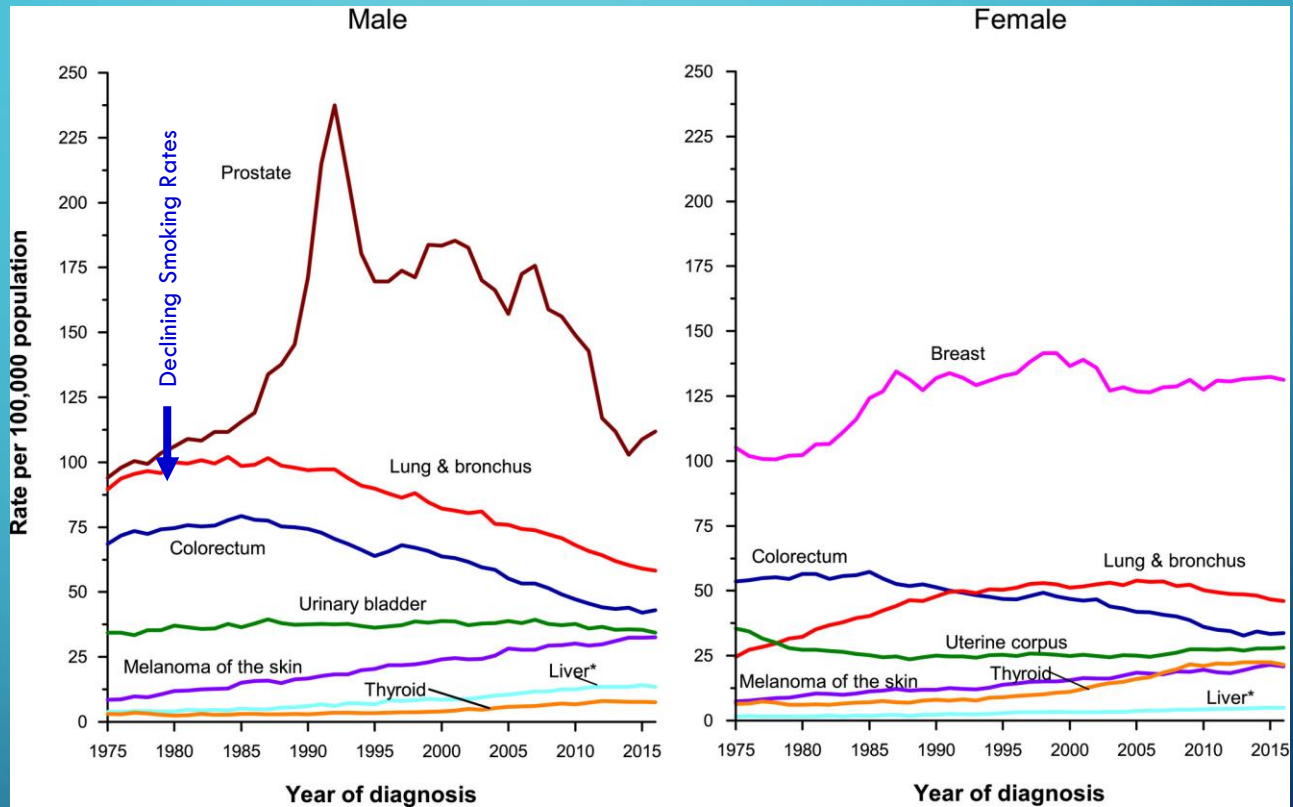
CANCER DEATHS IN THE UNITED STATES OF AMERICA (2020)			
	MALE	FEMALE	Ratio
All sites	321,160	285,360	1.1
CANCER SITE			
Esophagus	13,100	3,070	4.3
Larynx	3,000	750	4.0
Other oral cavity	1,270	350	3.6
Pharynx	2,820	820	3.4
Other nonepithelial skin	3,420	1,210	2.8
Oral cavity & pharynx	7,760	2,990	2.6
Tongue	1,980	850	2.3
Skin (excluding basal & squamous)	8,030	3,450	2.3
Urinary system	23,540	10,280	2.3
Other respiratory organs	870	390	2.2
Melanoma of the skin	4,610	2,240	2.1
Kidney & renal pelvis	9,860	4,970	2.0
Liver & intrahepatic bile duct	20,020	10,140	2.0
Mouth	1,690	970	1.7
Ureter & other urinary organs	630	380	1.7
Stomach	6,650	4,360	1.5
Other leukemic	3,090	2,120	1.5
Chronic myeloid leukemia	670	460	1.5
Hodgkin lymphoma	570	400	1.4
Digestive system	97,560	70,230	1.4
Bones & joints	1,000	720	1.4
Leukemia	13,420	9,680	1.4
Acute myeloid leukemia	6,470	4,710	1.4
Lymphoma	12,030	8,880	1.4
Non-Hodgkin lymphoma	11,460	8,480	1.4
Chronic lymphocytic leukemia	2,330	1,730	1.3
Acute lymphocytic leukemia	860	660	1.3
Brain & other nervous system	10,190	7,830	1.3
Myeloma	7,190	5,640	1.3
Small intestine	940	760	1.2
Respiratory system	76,370	64,360	1.2
Eye & orbit	210	180	1.2
Soft tissue (including heart)	2,870	2,480	1.2
Lung & bronchus	72,500	63,220	1.1
Other endocrine	560	520	1.1
Thyroid	1,040	1,140	0.9
Gallbladder & other biliary	1,700	2,390	0.7
Anus, anal canal, & anorectum	540	810	0.7
Breast	520	42,170	0.0
Prostate	33,330	-	-
Testis	440	-	-
Penis & other genital, male	440	-	-
Uterine cervix	-	4,290	-
Uterine corpus	-	12,590	-
Ovary	-	13,940	-
Vulva	-	1,350	-
Vagina & other genital, female	-	1,450	-

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CANCER STATISTICS 2020

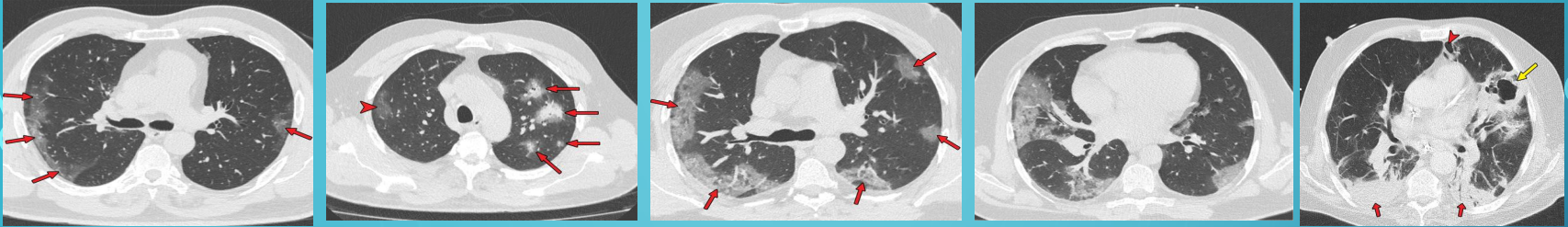


CA: A Cancer Journal for Clinicians, Volume: 70, Issue: 1, Pages: 7-30, First published: 08 January 2020, DOI: (10.3322/caac.21590)



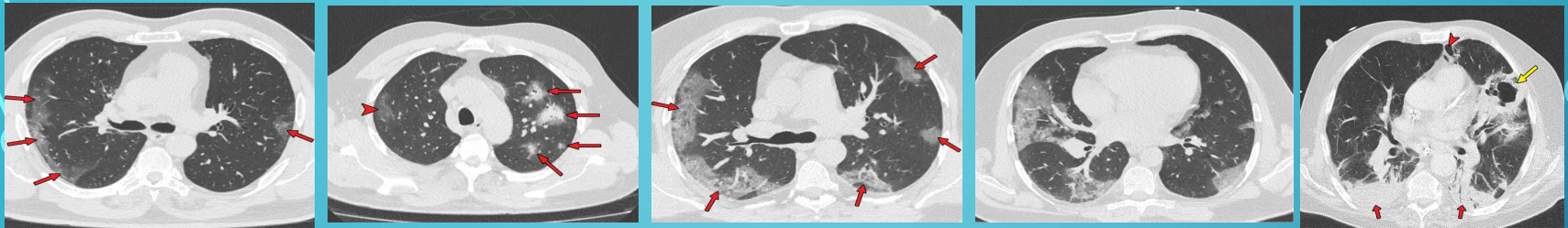
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ABNORMAL CHEST CT SCANS



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ABNORMAL CHEST CT SCANS



Covid-19 Lungs

Chest CT in COVID-19: What the Radiologist Needs to Know. Kwee CT Kwee RM. RadioGraphics, Published Online:Oct 23 2020<https://doi.org/10.1148/rg.2020200159>

Asymptomatic

Death



Lung Cancers

<https://www.semanticscholar.org/paper/CT-features-of-bronchiolo-alveolar-carcinoma-Kirova-Simidchiev/6eb1bf81f731605f397f50fb9c02f10c027590a9>

<https://www.cureus.com/articles/27111-a-rare-case-of-non-small-cell-lung-cancer-with-braf-v600e-gene-case-report-and-literature-review>

Tannous T, Mak A, Keating M (March 04, 2021) Small-Cell Lung Cancer Cavities: Primary or Secondary?. Cureus 13(3): e13691. doi:10.7759/cureus.13691

https://cdn.amegroups.cn/static/magazine_modules/imgRender/dist/index.html?imgSource=https://cdn.amegroups.cn/journals/pbpc/files/journals/2/articles/27742/public/27742-PB14-4713-R1.png

<https://www.wjgnet.com/2218-4333/full/v11/i7/WJCO-11-412-g003.htm>



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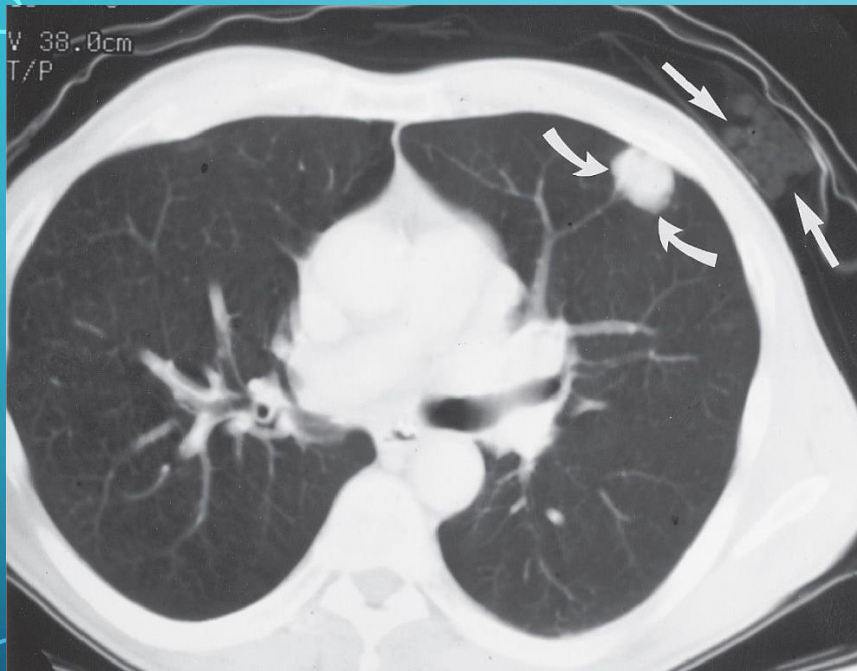
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TYPES OF LUNG CANCER

- NON-SMALL CELL
 - Adenocarcinoma (50% of all)
 - Strong association with smoking (70% are smokers)
 - Also the most common type in never-smokers
 - More common in women
 - Squamous (25% of all)
 - Previously the most common
 - Strongly associated with cigarette smoking (90% are smokers)
- SMALL CELL LUNG CANCER
 - Strongly linked to smoking (95% are smokers)
 - Decreasing frequency

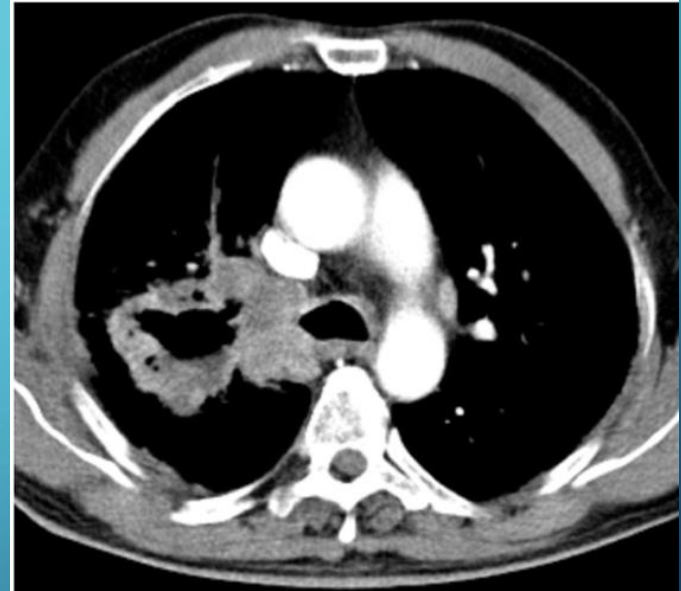
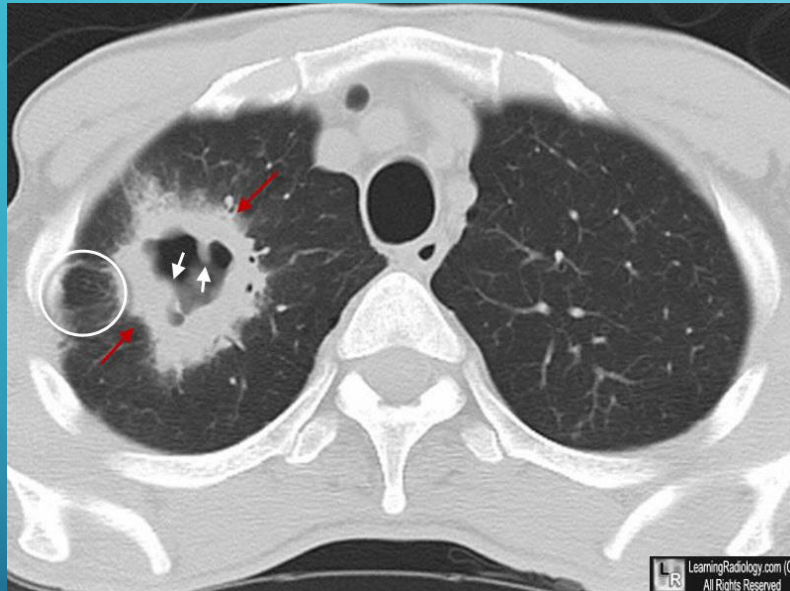


LUNG ADENOCARCINOMA



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SQUAMOUS CELL LUNG CANCER

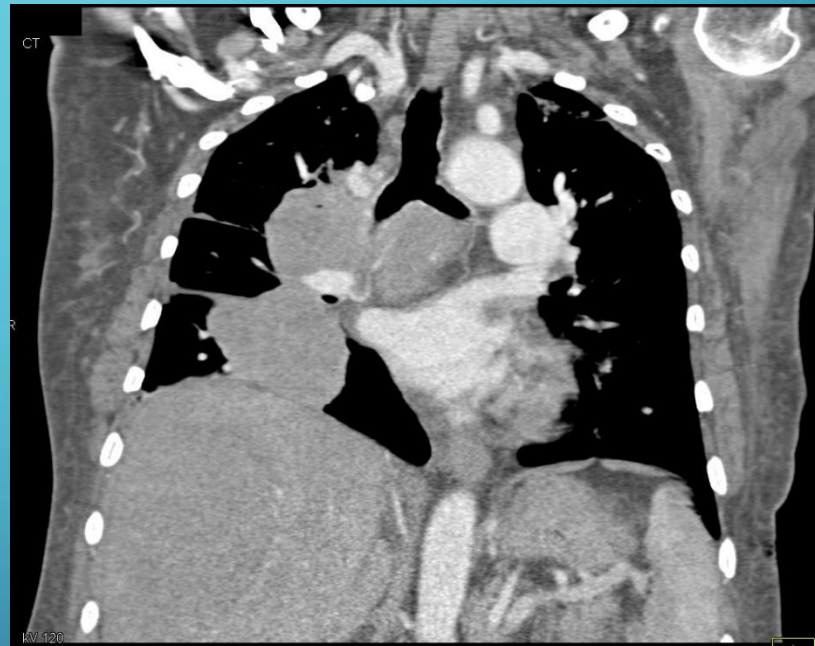


<https://ejb.springeropen.com/articles/10.1186/s43168-020-00027-w/figures/1>



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SMALL CELL LUNG CANCER

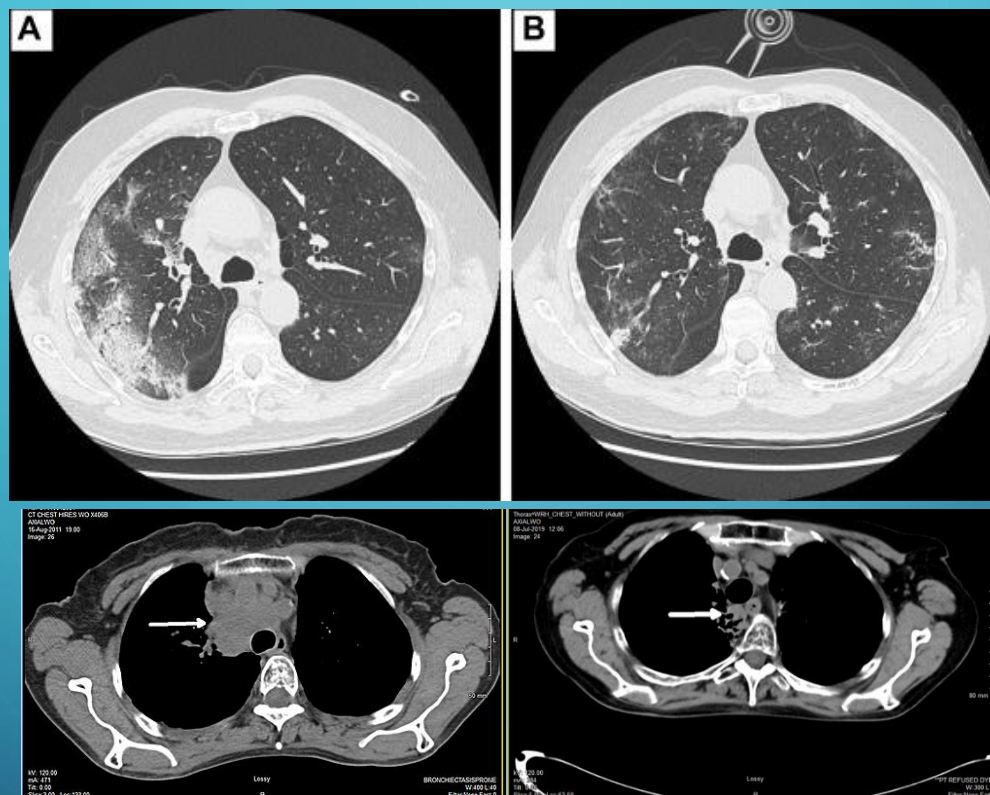


<https://ctisus.com/responsive/teachingfiles/chest/269488>



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SMALL CELL LUNG CANCER AFTER CHEMOTHERAPY



[https://www.clinical-lung-cancer.com/article/S1525-7304\(20\)30254-0/fulltext](https://www.clinical-lung-cancer.com/article/S1525-7304(20)30254-0/fulltext)



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MESOTHELIOMA



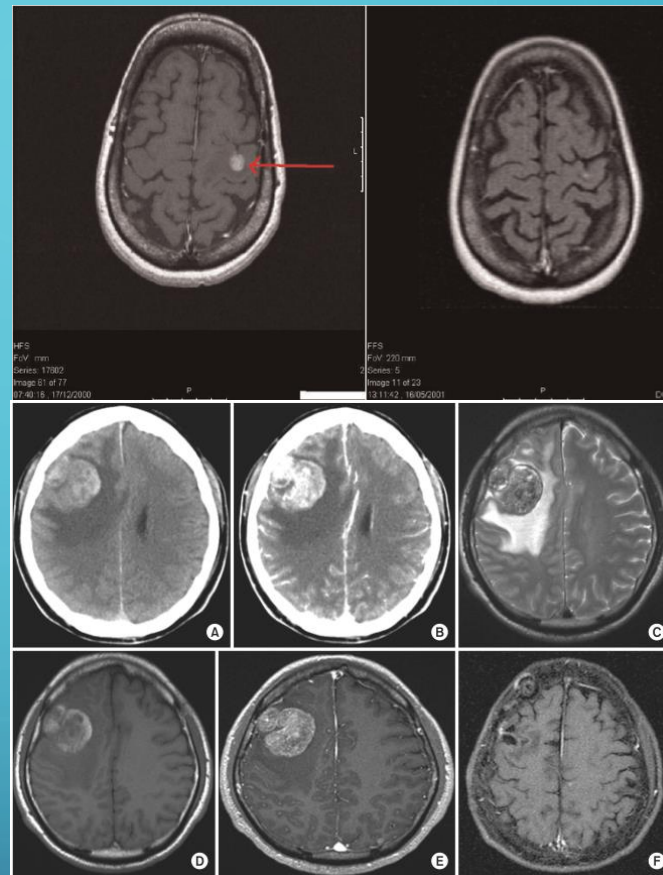
DU CANE MEDICAL IMAGING LTD / SCIENCE PHOTO LIBRARY



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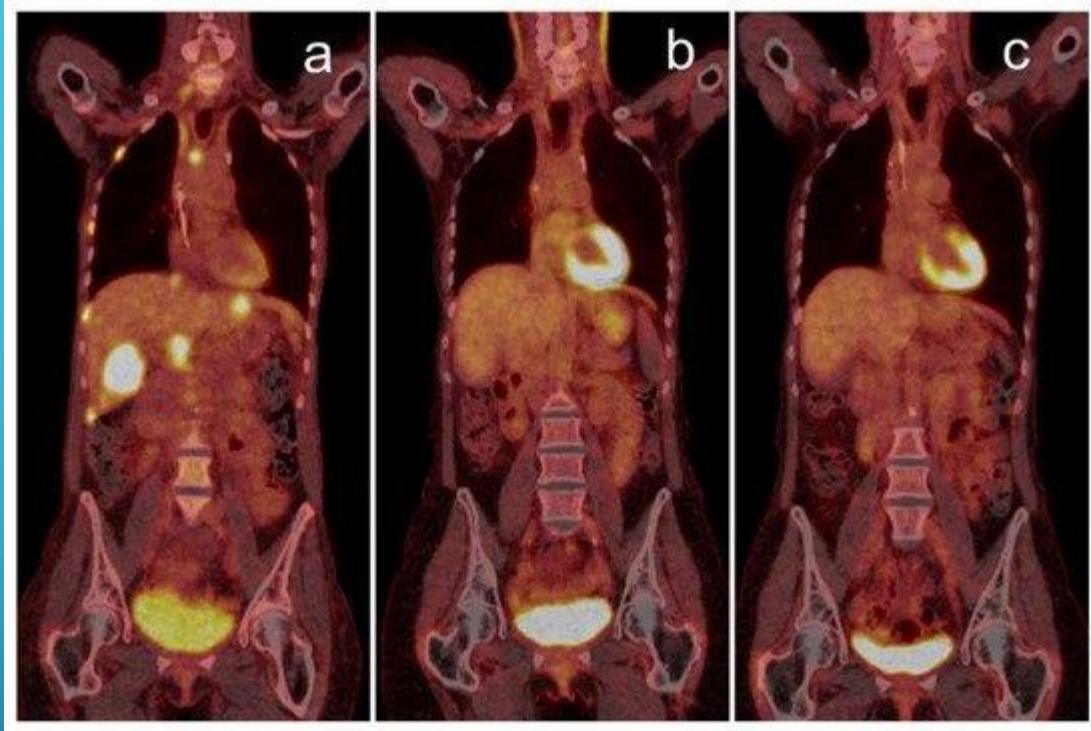
BRAIN METASTASES

https://www.researchgate.net/figure/Illustrative-case-A-55-yr-old-male-with-non-small-cell-lung-cancer-with-hemorrhagic_fig4_51542403



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LIVER METASTASES



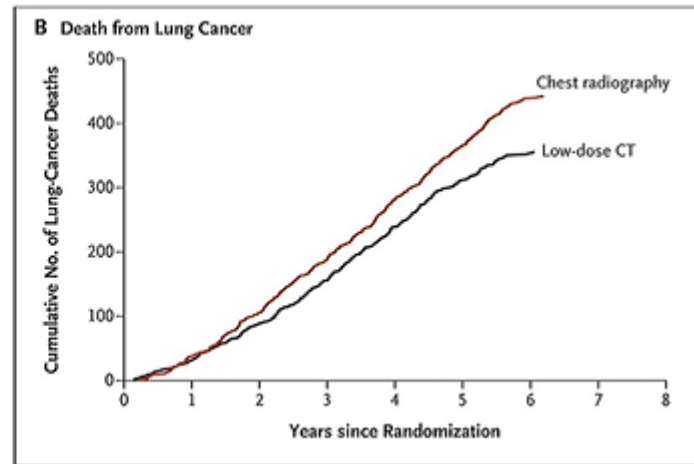
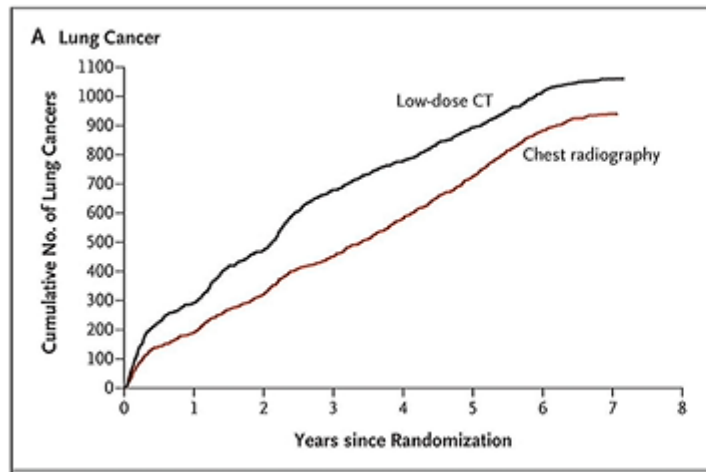
Resolution of liver metastases of squamous cell lung cancer
with immunotherapy



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LOW-DOSE, HIGH-RESOLUTION CT SCANS FOR EARLY DETECTION

National Lung Screening Trial



Aberle et al. *N Engl J Med.* 365:395, 2011



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LOW-DOSE, HIGH-RESOLUTION CT SCANS FOR EARLY DETECTION

Dutch-Belgian Screening Trial

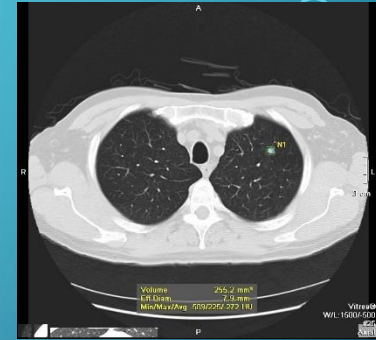
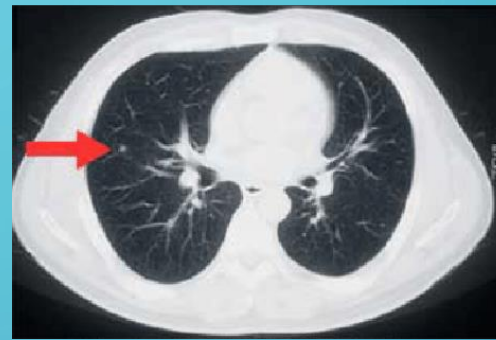
Lung Cancer mortality rate ratio (95% CI)	Year 8	Year 9	Year 10
Males (84%)	0.75 P=0.015 (0.59-0.95)	0.76 P=0.012 (0.60-0.95)	0.74 P=0.003 (0.60-0.91)
Females (16%)	0.39 P=0.0037 (0.18-0.78)	0.47 P=0.0069 (0.25-0.84)	0.61 P=0.0543 (0.35-1.04)

de Koning et al. New Engl J Med epub January 29, 2020



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SCREENING CT CHEST



Pua, B. CT scans lower lung cancer deaths, according to study. Cornell Univesity. <https://medicalxpress.com/news/2014-07-ct-scans-lung-cancer-deaths.html>

<https://www.foxchase.org/blog/20130131-lung-cancer-screening-recommendations-from-the-acs>

Alakwaa W et al., Lung Cancer Detection and Classification with 3D Convolutional Neural Network (3D-CNN). - International Journal of Advanced Computer Science and Applications

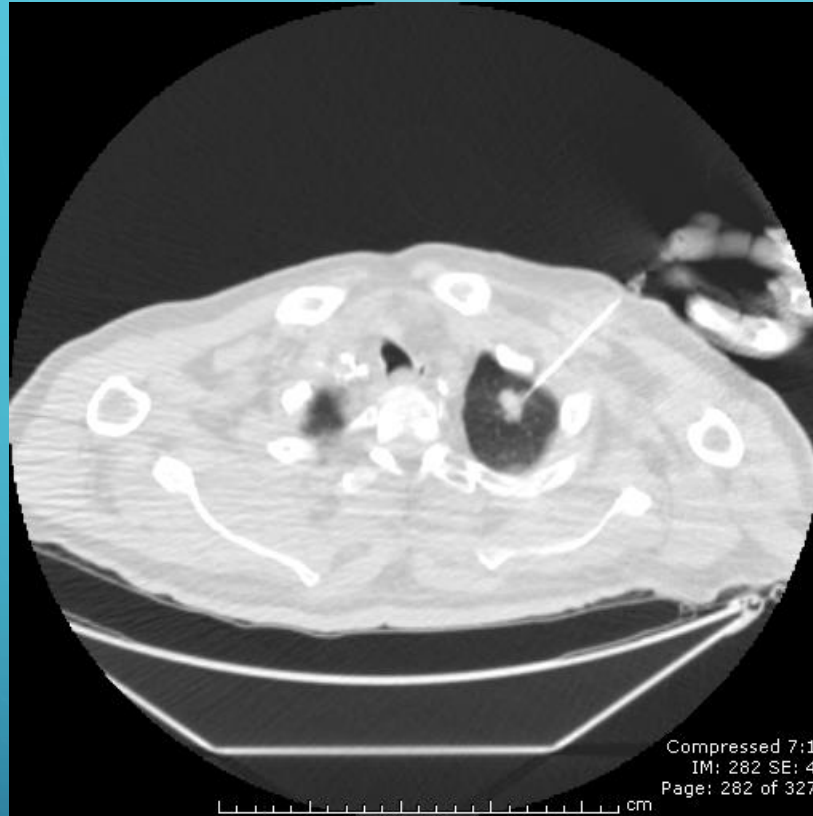
DOI - 10.14569/IJACSA.2017.080853

<http://www.rad.pitt.edu/node/242>



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CT-GUIDED LUNG BIOPSY



<https://www.cancernetwork.com/view/slide-show-non-small-cell-lung-cancer-imaging?page=2>



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WHO SHOULD HAVE LUNG CANCER SCREENING

Have a 20 pack-year or more smoking history and smoke now or have quit within the past 15 years and are between 50 and 80 years old.

A pack-year is smoking an average of one pack of cigarettes per day for one year. For example, a person could have a 20 pack-year history by smoking one pack a day for 20 years or two packs a day for 10 years.

Centers for Disease Control and Prevention. CDC twenty four seven. Saving Lives, Protecting People Centers for Disease Control and Prevention.



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WHO SHOULD HAVE LUNG CANCER SCREENING

Recommendations: American College of Chest Physicians, ASCO, and US Preventive Services Task Force

- *The United States Preventive Services Task Force recommends annual screening for lung cancer with low-dose computed tomography in adults ages 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years.
- The Centers for Medicare & Medicaid Services (CMS) has determined that the evidence is sufficient to add a lung cancer screening counseling and shared decision making visit, and for appropriate beneficiaries, annual screening for lung cancer with low dose computed tomography (LDCT), as an additional preventive service benefit under the Medicare program (February 15, 2015)
- The current CT screening rates are only about 6% of the eligible patients in the US in 2015.

*www.uspreventiveservicestaskforce.org/uspstf/uspstlung.htm, Ann.Intern Med 160:I-40-40, 2014

Jemal et al JAMA Oncol 3:1278, 2017

https://progressreport.cancer.gov/detection/lung_cancer

<https://www.cdc.gov/cancer/dcpc/research/articles/lung-cancer-screening.htm>



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EARLY DIAGNOSIS OF LUNG CANCER BY A BLOOD TEST

NHS Early detection of Cancer of the Lung Scotland (ECLS)
EarlyCDT-Lung® blood test

36% reduction in late stage lung cancer compared to standard clinical practice - a statistically significant reduction compared to the current NHS standard of care.

There were nonsignificant differences in lung cancer and all-cause mortality after 2 years.

Stay tuned...

Earlier diagnosis of lung cancer in a randomised trial of an autoantibody blood test followed by imaging. Sullivan EM, et al., Eur Respir J. 2021 Jan 14;57(1):2000670.
Lung Cancer Scotland (ECLS) Team



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EARLY DIAGNOSIS OF LUNG CANCER BY A BLOOD TESTS

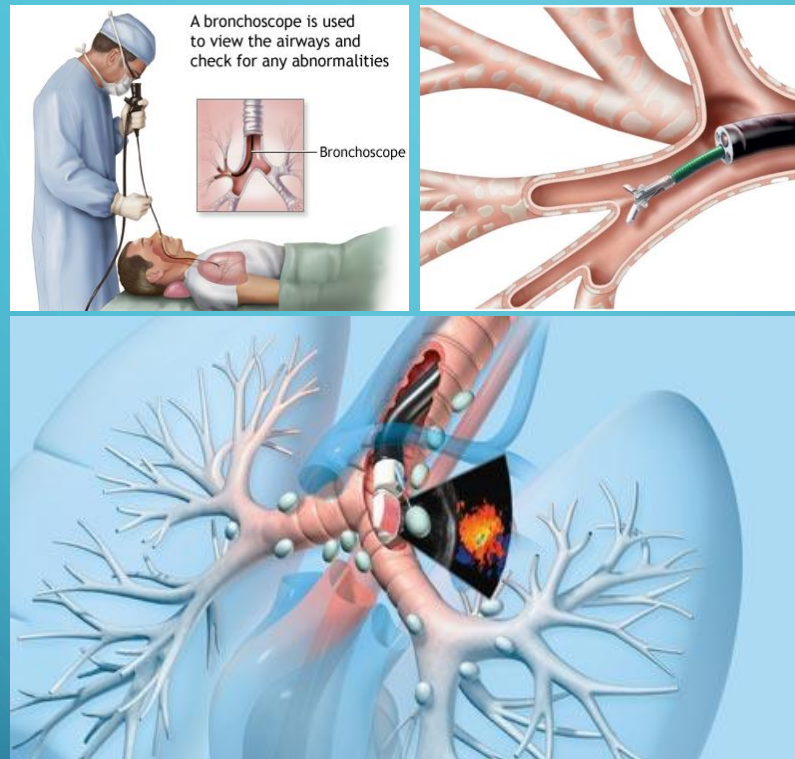
Detection and characterization of lung cancer using cell-free DNA fragmentomes
Mathios D., et al., Nature Communications volume 12, Article number: 5060 (2021)

Liquid biopsy for lung cancer early detection. Santarpia, M et al., Journal of Thoracic Disease, 2018; 10(Supplement 7)April 2018/ Review Article



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BRONCHOSCOPIC BIOPSY



<https://medlineplus.gov/ency/article/003857.htm>

<https://qldrespiratorysleep.com.au/advanced-bronchoscopy/>



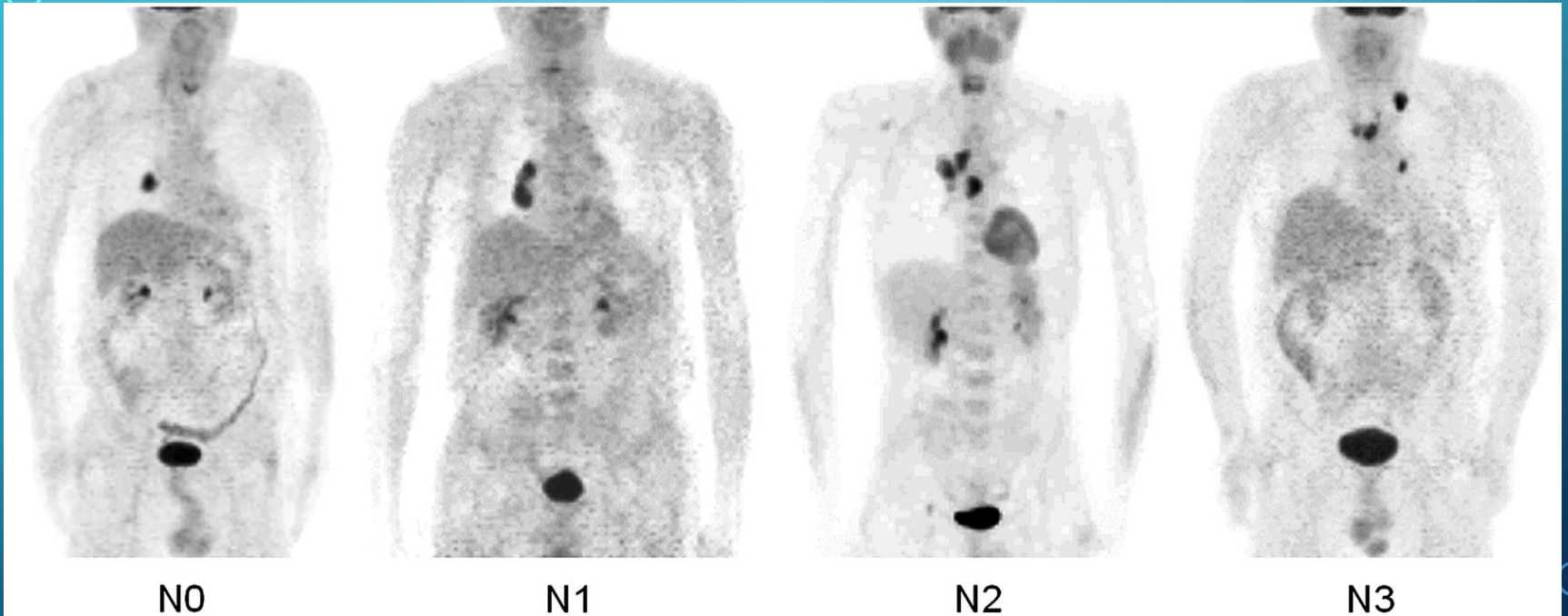
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SURGICAL TREATMENT OF EARLY STAGE LUNG CANCER

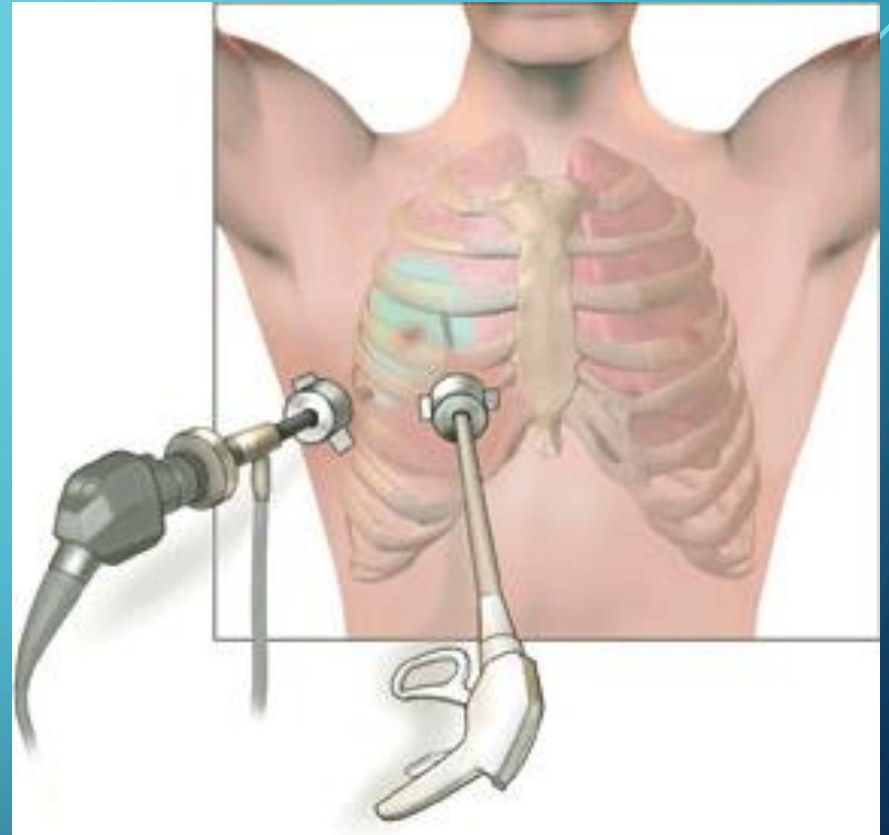
- Pulmonary Functions
- Positron Emission Tomography (PET-CT scan)
- MRI brain
- If no evidence of spread, surgical removal
- Lobectomy



PET-SCAN FOR STAGING SPREAD TO LYMPH NODES



VIDEO-ASSISTED THORACOSCOPIC RESECTION (VATS): MINIMALLY INVASIVE SURGERY

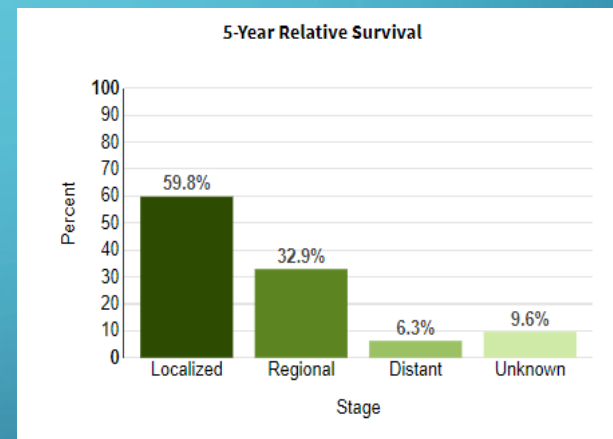
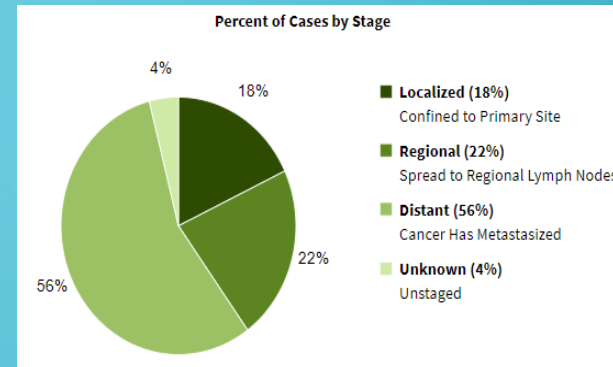


<https://columbiasurgery.org/conditions-and-treatments/thoracic-minimally-invasive-and-video-assisted-surgery-vats>



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STAGES OF LUNG CANCER



STAGE IIIA LUNG CANCER

- Preoperative Chemotherapy
- Pre-operative Chemotherapy with Radiation
- Pre-operative Immunotherapy
- Pre-operative Immunotherapy with Radiation
- Pre-operative Immunotherapy with Chemotherapy
- Pre-operative Immunotherapy with Chemotherapy and Radiation
- FOLLOWED BY SURGERY IF POSSIBLE



STAGE IIIB LUNG CANCER

- Pre-operative Chemotherapy with Radiation
- Pre-operative Immunotherapy with Radiation
- Immunotherapy with Chemotherapy and Radiation
- USUALLY NO SURGERY



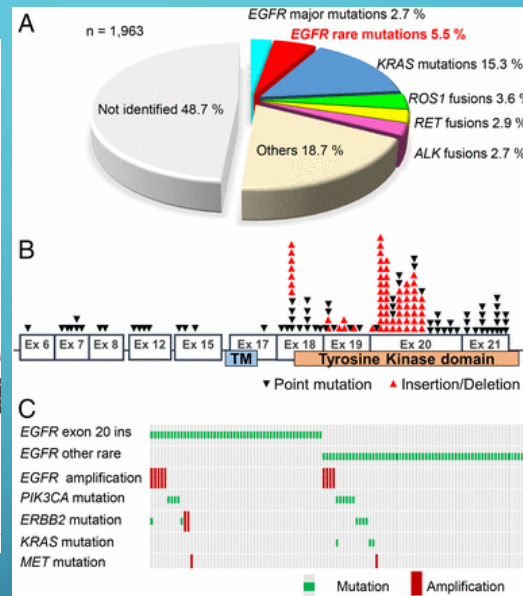
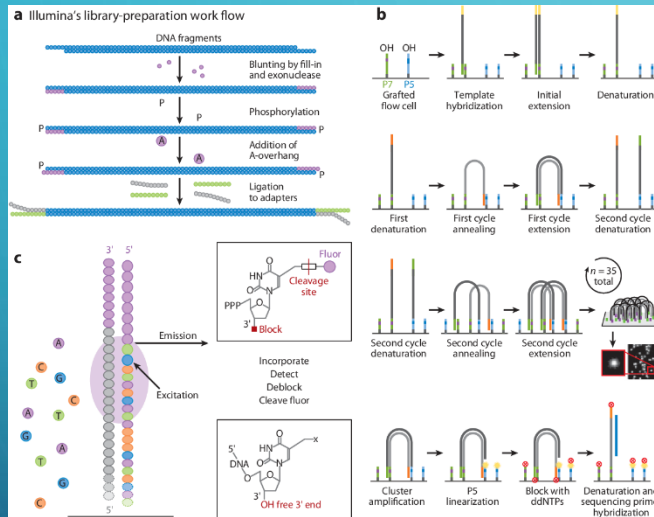
STAGE IV

- Radiation for specific reasons (i.e. to control symptoms)
- Systemic Treatment (oral or IV)
 - Chemotherapy
 - Natural Products
 - Platinum
 - Alkylating Agents
 - Epigenetic Modifiers
 - Signal Transduction Inhibitors
 - Cell-surface Receptor-targeting Antibodies (MABs)
 - Intracellular kinase and G-protein inhibitors
 - Tumour-suppressor Activators (p53- Guardian of the Genome)
 - Endocytosis Inhibitors
 - Apoptosis Activators
- Combinations
- Clinical Trials



SIGNAL TRANSDUCTION INHIBITORS – NIBS/MABS

Next-Gen Sequencing and Tailored Therapy



Gefitinib

Erlotinib

Afatinib

Osimertinib

Certinib

Alectinib

Brigatinib

Lorlatinib

Cetuximab

Panitumumab

Necitumumab

Trastuzumab

Pertuzumab

Bevacizumab

Ramucirumab

Ado-trastuzumab Emtansine

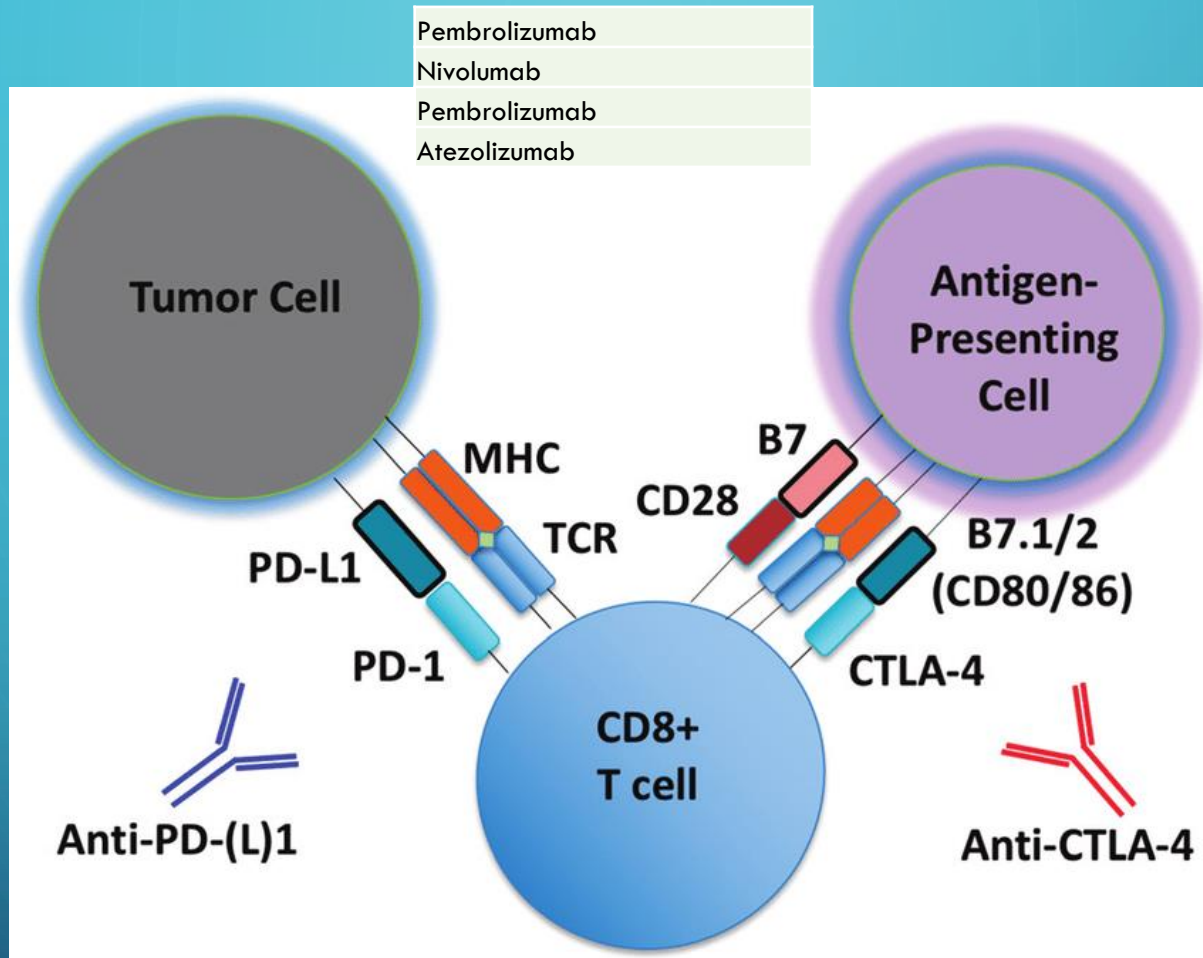
Dinutuximab



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PD1, PD-L1 AND CTLA4 ANTIBODIES



TAKE HOME MESSAGE

- Prevention is the Key to the Best Kind of Cancer-free Survival
- Early Detection is the Key to Cure
- Major Advances in the Past 2 Decades Have Radically Changed Cancer Treatment
- Hiding Your Head In the Sand is Likely to Cause its Severing
- A Little Knowledge is a Dangerous Thing
- An opinion is worth what you pay for it
- THROUGH EARLY DETECTION CANCER IS CURABLE



COVID-19 – THE SOAPBOX SPEECH

I HAVE SEEN IT FIRST HAND – YOU DO NOT WANT IT IN PARADISE!

THE SAME TECHNOLOGY AND KNOWLEDGE THAT HAS CURED MANY, MANY CANCERS HAS YIELDED THE REVOLUTIONARY TECHNOLOGY THAT HAS GIVEN US THE MOST EFFECTIVE VACCINES OF ALL TIME – AND IN RECORD TIME

QUIT THE PARANOIA – IT DOES NOT SUIT YOU

IT IS NOT JUST ABOUT YOU

SELFISHNESS VS. SACRIFICE

THE ONLY THING WE HAVE TO FEAR IS FEAR ITSELF

DON'T BE CHICKEN _ _ _ _ . GET VACCINATED

BECAUSE I HAVE THESE SCARS, OUR CHILDREN WON'T GET THESE



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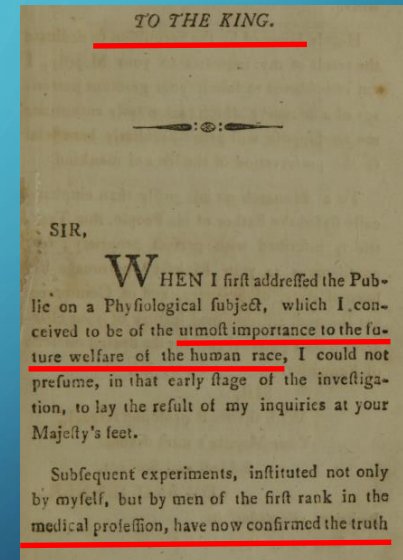
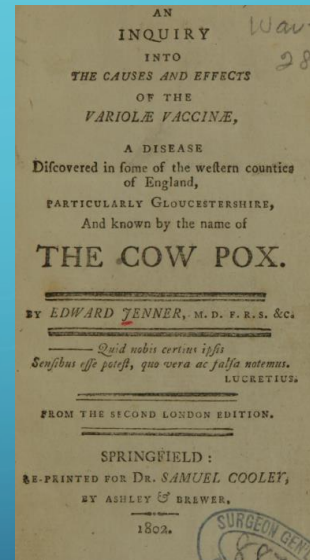
IN ACQUIRING THE VAST KNOWLEDGE AVAILABLE ON SOCIAL MEDIA ABOUT THE KARDASHIANS AND KANYE, WE SEEM TO HAVE FORGOTTEN ABOUT CIVIC DUTY AND THE MILK MAID'S TALE.....



Consider Reading

Edward Jenner and the history of smallpox and vaccination

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1200696>



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SINCERE THANKS FOR YOUR ATTENTION

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