

# Breast cancer

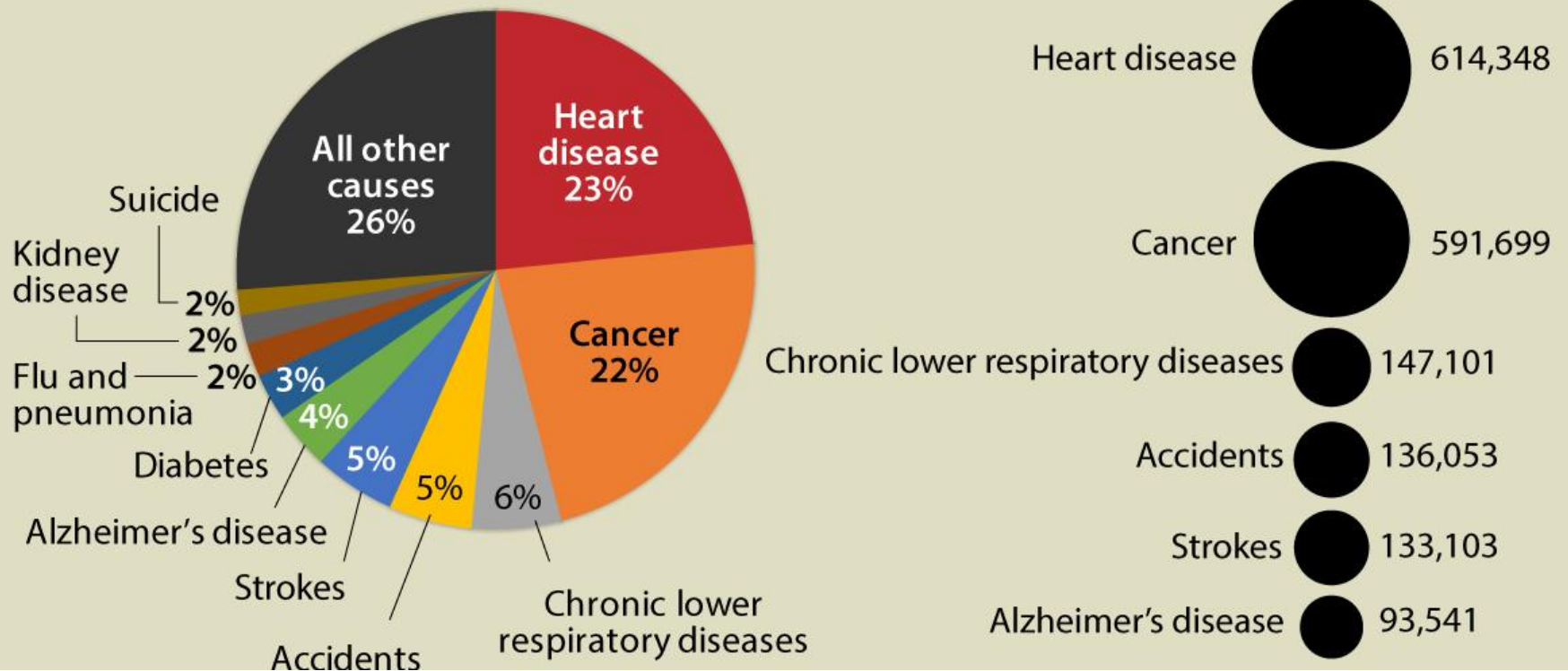


**Peter Grell, Miloš Holánek**

Masaryk Memorial Cancer Institute  
Faculty of Medicine, Masaryk University  
Brno

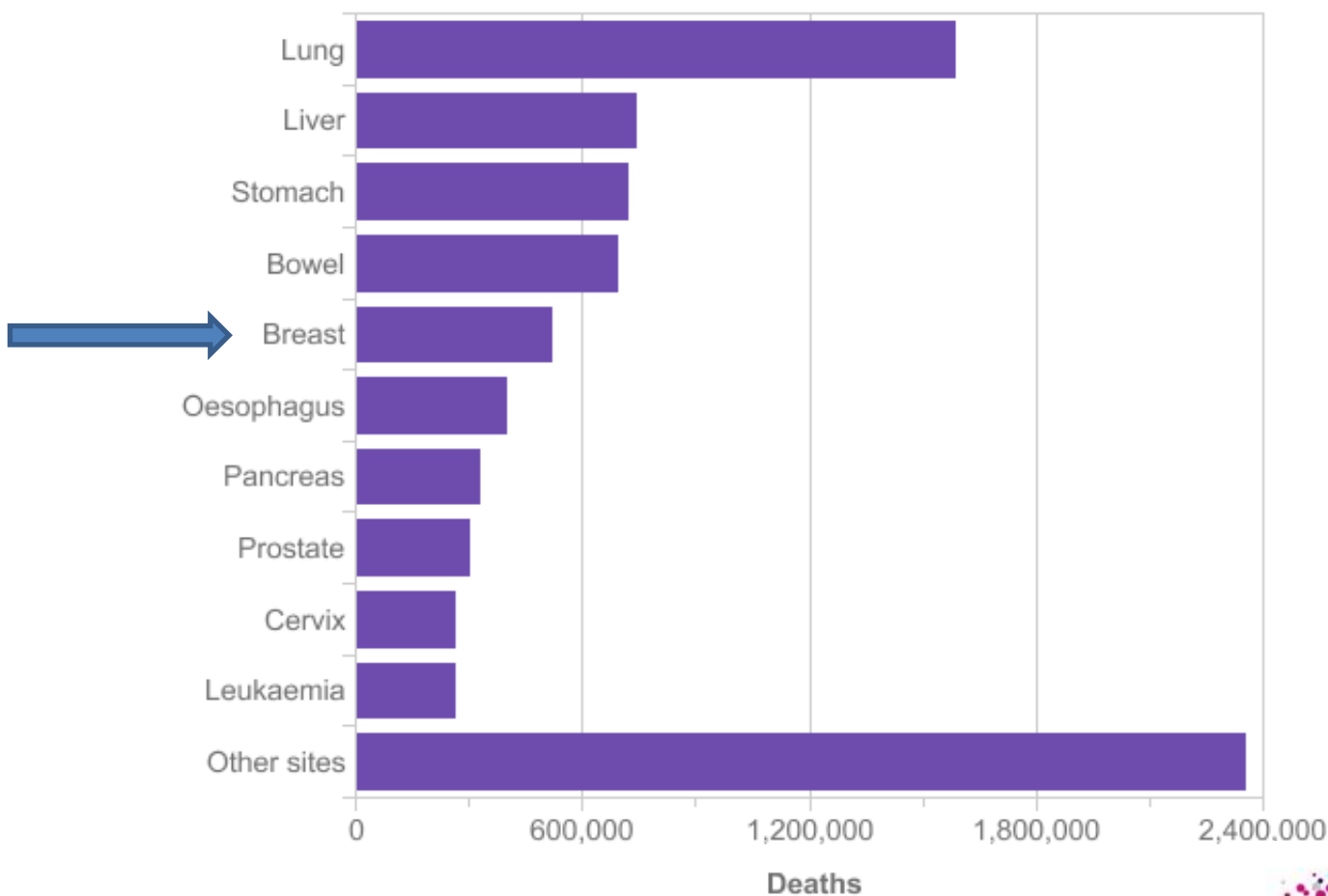
# TOP KILLERS - 2014

In 2014, 2,626,418 people (out of a total U.S. population of 318,857,056) died of all causes. Here is the breakdown of the top 10 killers:



## The 10 Most Common Causes of Cancer Death: 2012 Estimates

### Total Number and Percentage of Deaths from Cancer per Year, Worldwide



Bowel including anus, ICD 10 C18-C21

Please include the citation provided in our Frequently Asked Questions when reproducing this chart: <http://info.cancerresearchuk.org/cancerstats/faqs/>

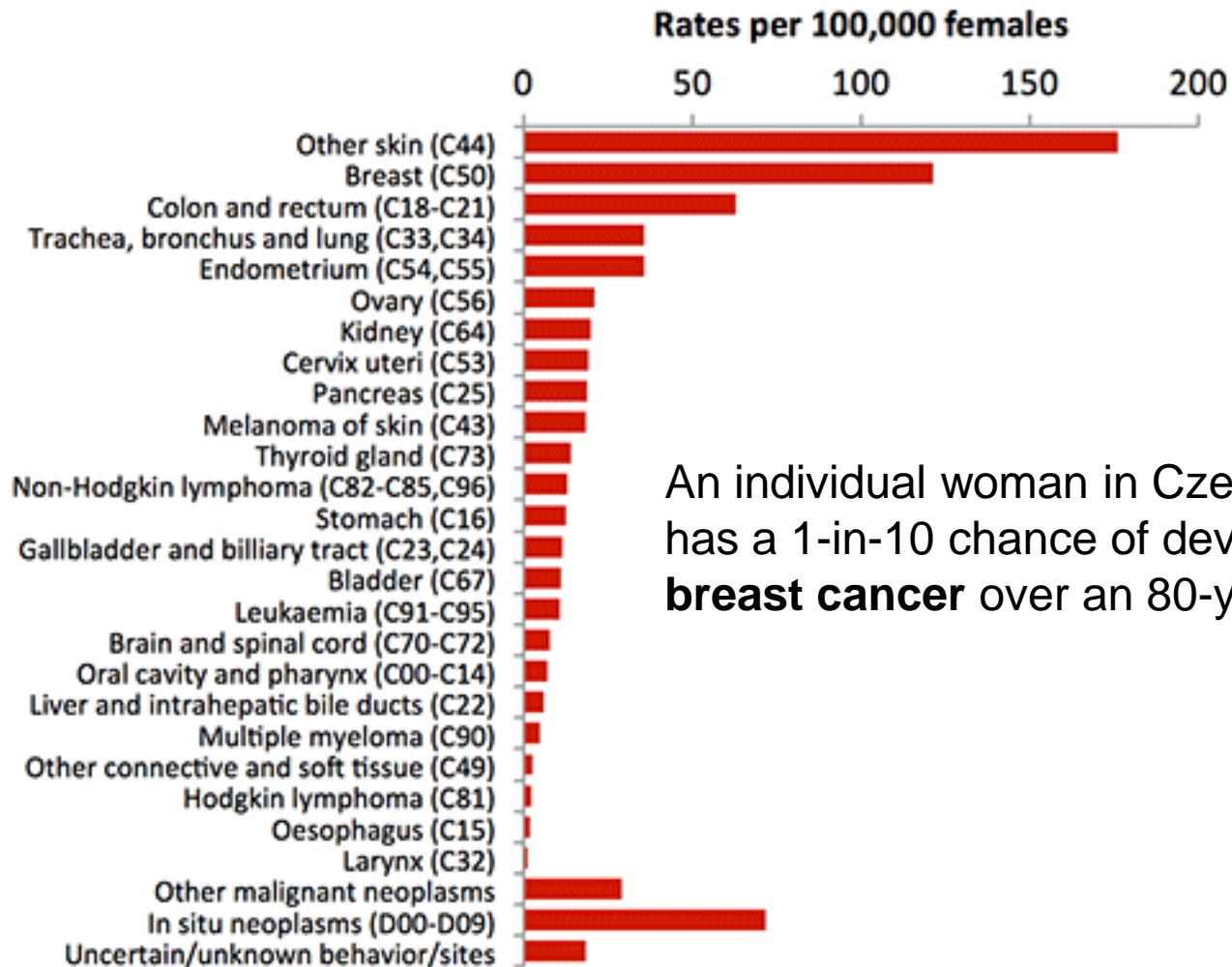
Prepared by Cancer Research UK

Original data sources:

Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray, F. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: <http://globocan.iarc.fr>, accessed on 16/01/2014.



# Cancer rates in Czech republic



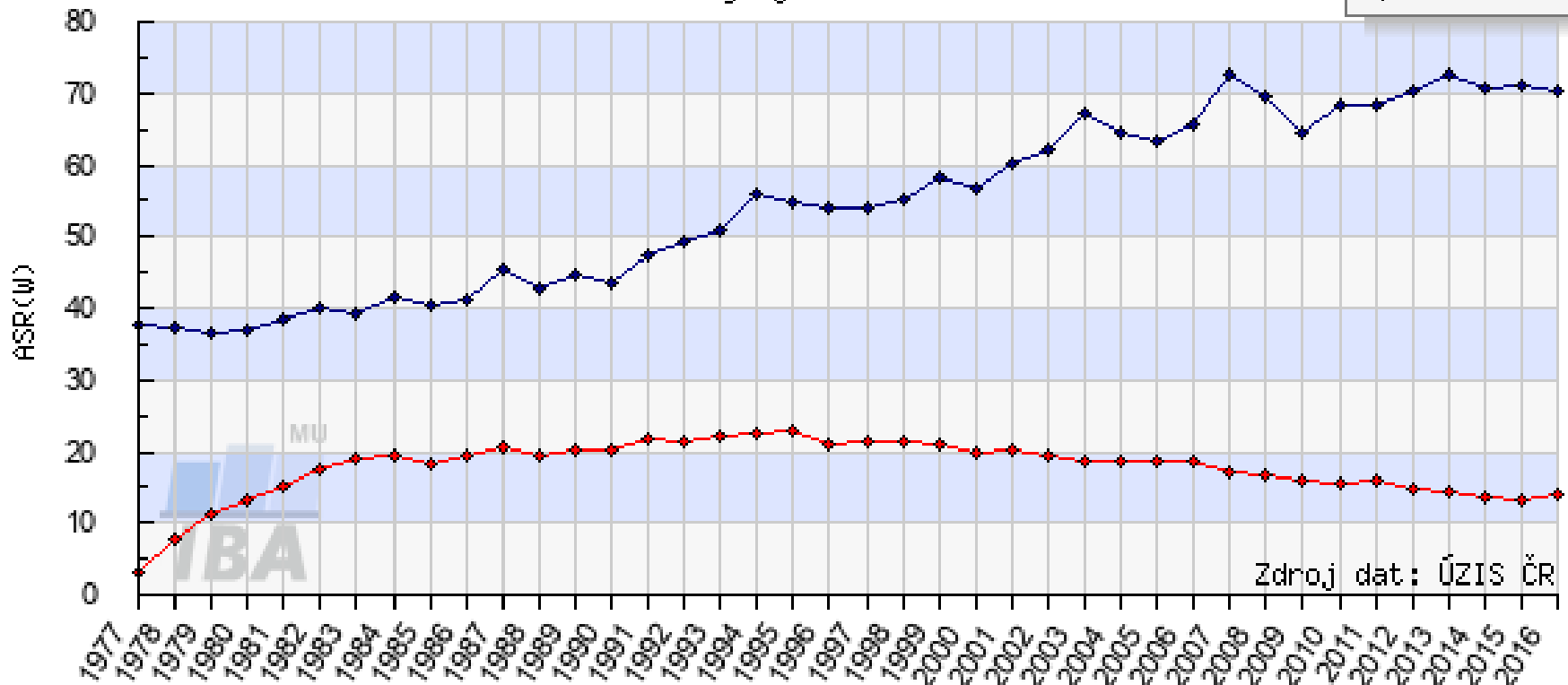
An individual woman in Czech Republic has a 1-in-10 chance of developing **breast cancer** over an 80-year lifespan

# Incidence nad mortality in Czech Republic

C50 - ZN prsu, ženy

Vývoj v čase

◆ Incidence  
◆ Mortalita



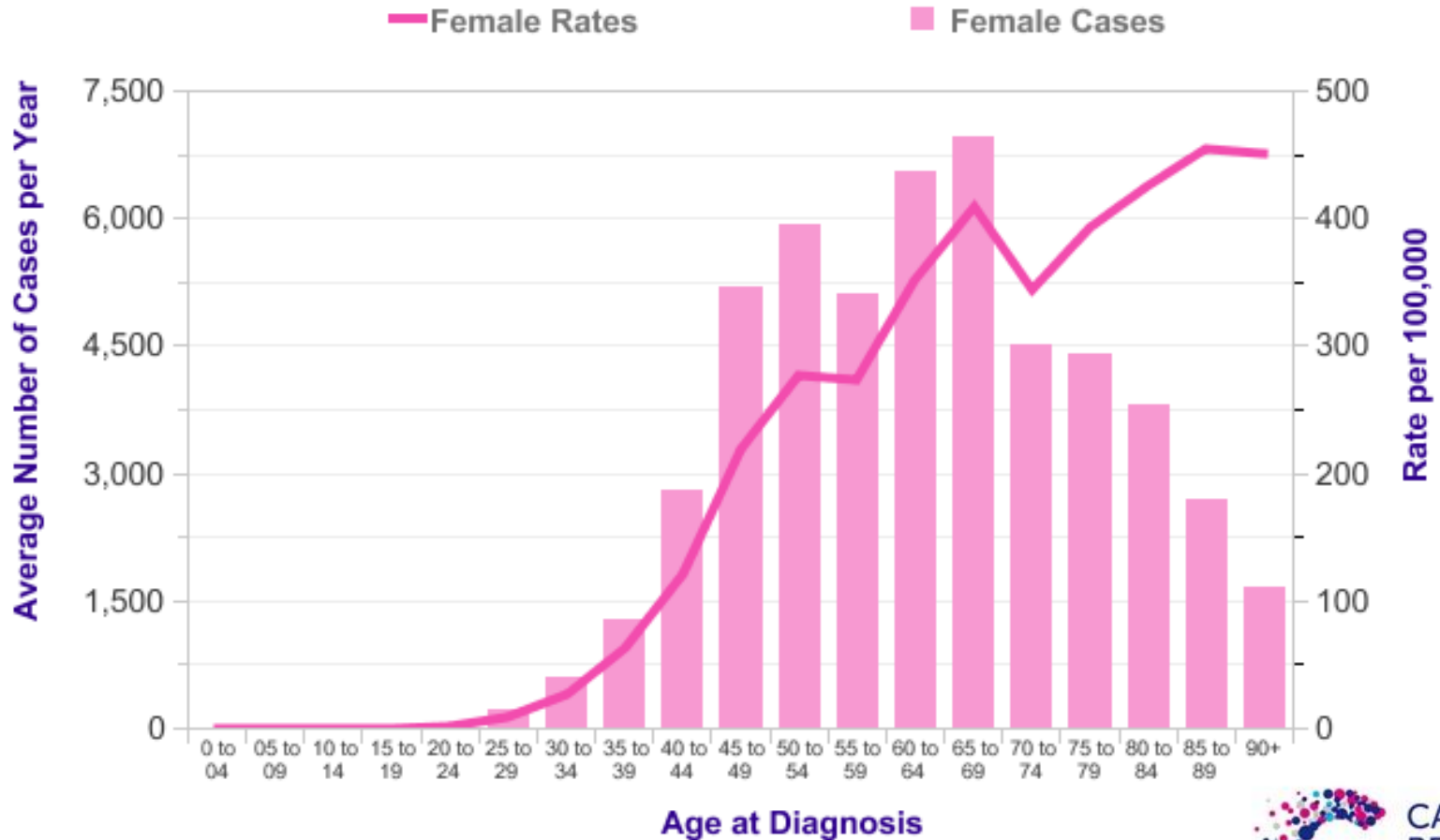
Analyzovaná data: N(inc)=192157, N(mor)=72182

Zdroj dat: ÚZIS ČR  
<http://www.svod.cz>

# Age-specific incidence of breast cancer

Breast Cancer (C50): 2011-2013

Average Number of New Cases Per Year and Age-Specific Incidence Rates per 100,000 Population, Females, UK



Source: [cruk.org/cancerstats](http://cruk.org/cancerstats)  
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# Clinical signs

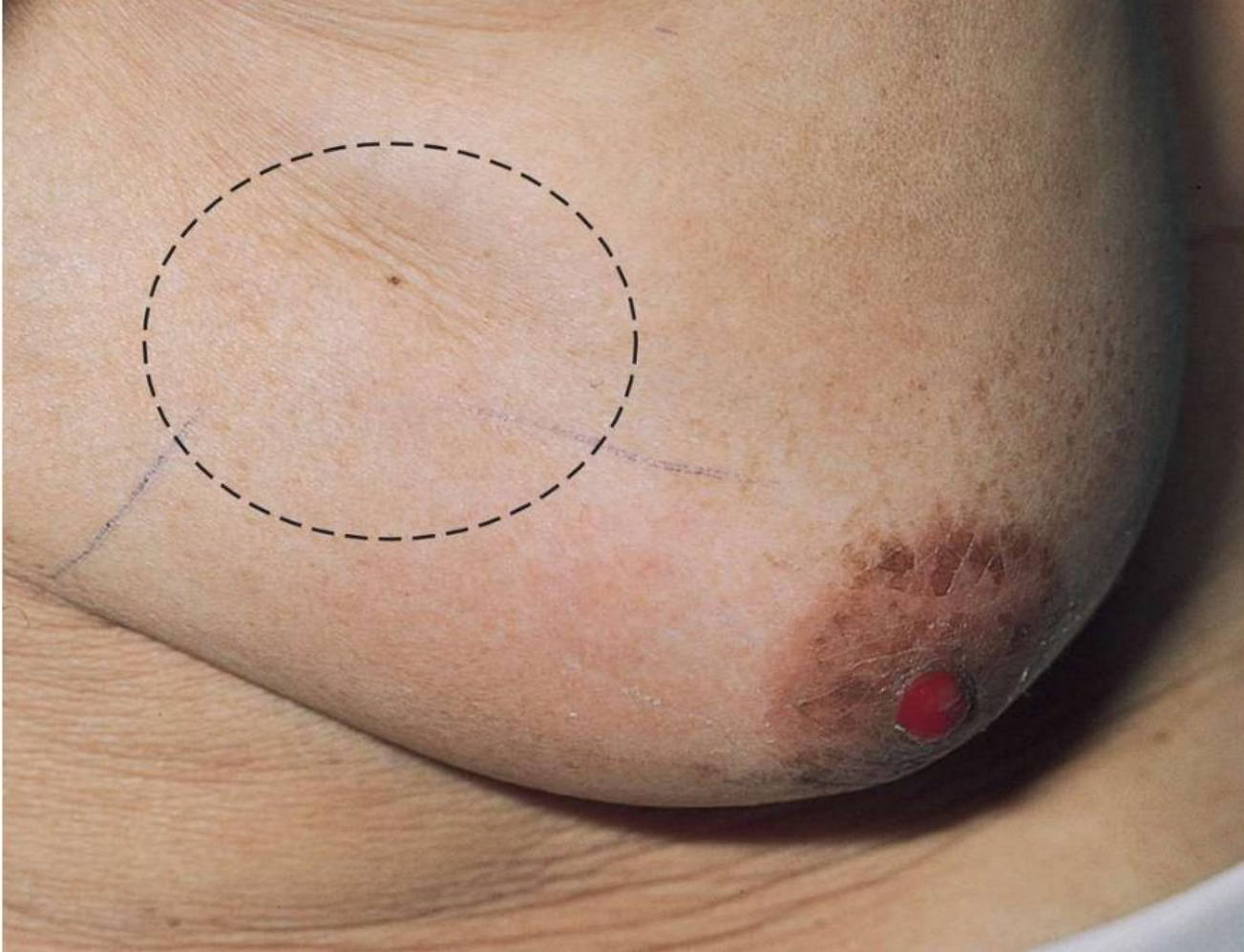
what does a patient show up with  
??

# Clinical signs

- Resistance in breast
  - most often in upper lateral quadrant
- Skin edema
- Erythematic skin
- Skin retraction, ulceration
- Inverted nipple
- Usually painless
- General symptoms: asthenia, weight loss, dyspnea



# Lump



# Large resistance

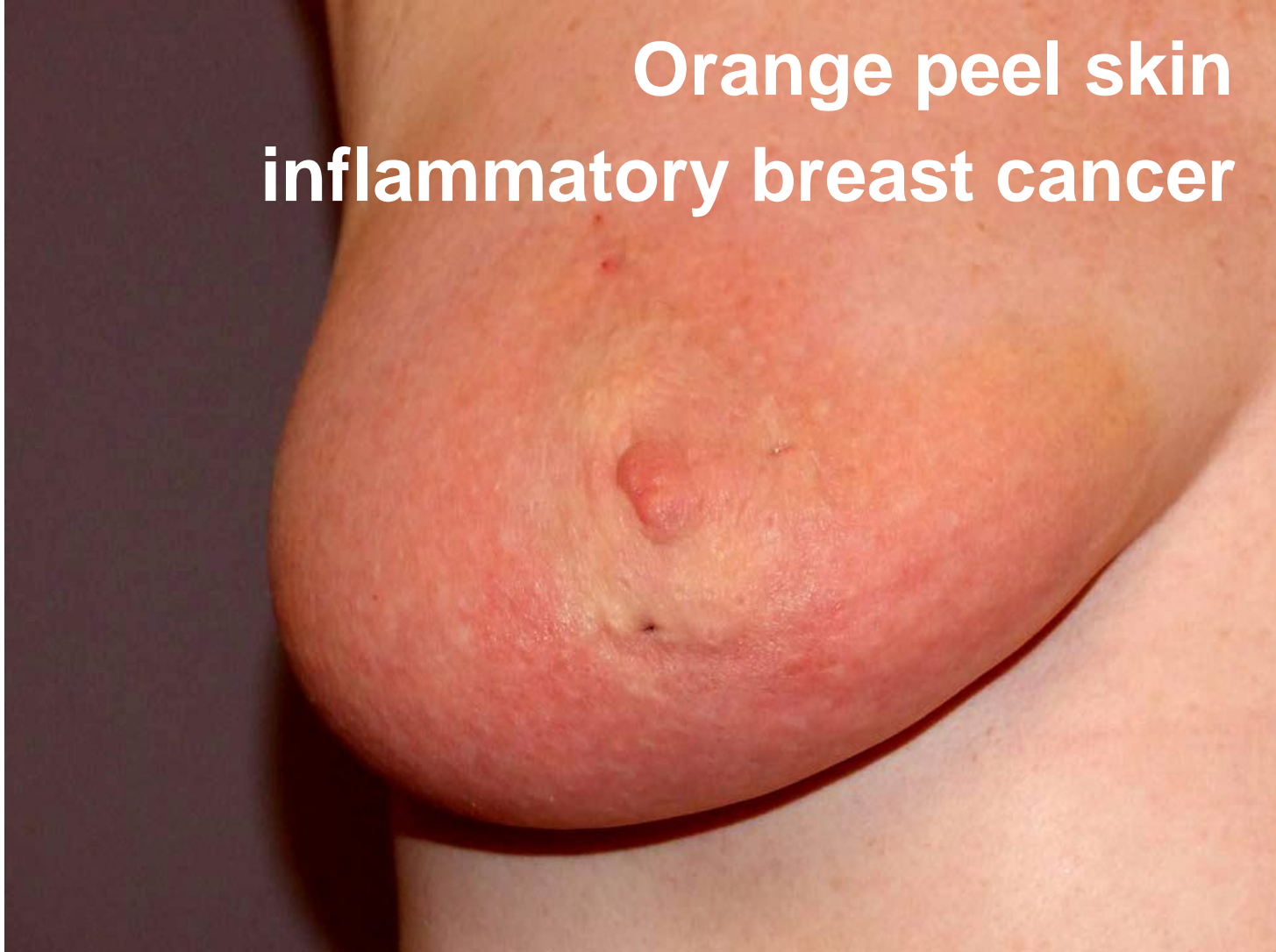


# Skin retraction



# Skin edema and erythema

**Orange peel skin  
inflammatory breast cancer**



# Inverted nipple



# **Risk factors**

or

**Can I do something to prevent cancer?**

# Risk factors

- **Positive family history:** breast cancer in 1st grade relatives
  - One relative                      1.5 to 2.0 times risk
  - Two relatives                      5.0 times
- **Early onset of menarche:** earlier than 12 years
- **Late onset of menopause:** after age of 55
- **Nulliparity**
- **Combined hormonal substitution (after menopause)**
- **Smoking, lack of physical activity, alcohol (shift work?)**
- **Benign breast afections:** Atypical ductal hyperplasia
- **Genetic factors,** responsible for 5-10 % of breast cancers

# Genetic risk factors

- BRCA1 a BRCA2 genes – responsible for DNA reparation - Homologous recombination
- Risk of breast cancer in woman with **BRCA1** mutation is 80%, ovarian canrer 60%, with **BRCA2** mutation 80%, and 25% respectively
- Only prevention is bilateral mastectomy + salpingo-oophorectomy

**Likelihood of a 25-year-old woman surviving to age 70**  
(without screening or medical interventions to prevent cancer)

<b>Group</b>	<b>Percentage surviving to age 70</b>
<i>BRCA1</i> mutation	53
<i>BRCA2</i> mutation	71
Typical woman	84



# Diagnostics

how do WE find out ??

?



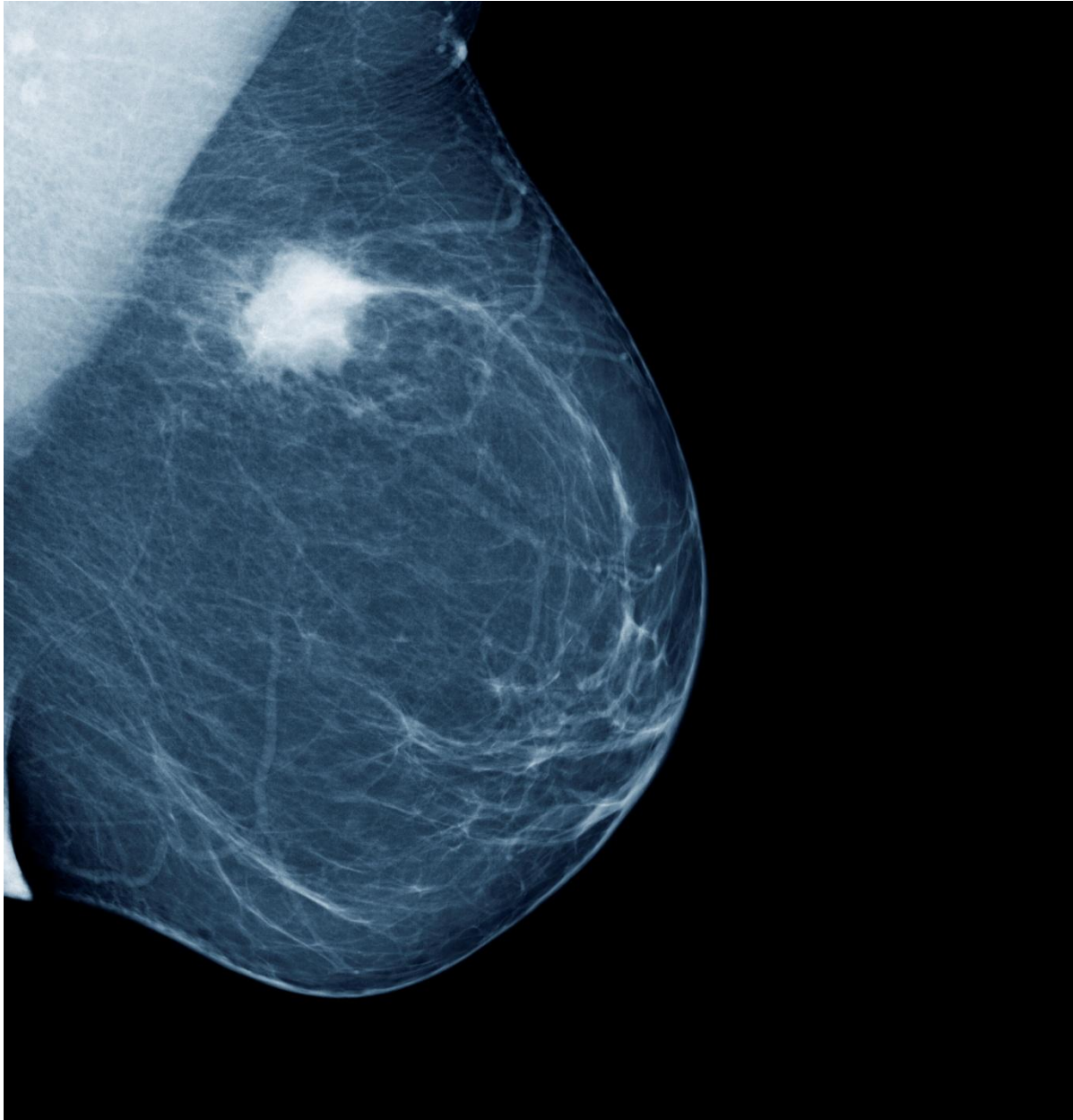
?

# Initial diagnosis

- Case 1:
- 62 year old women
- New resistance in left breast (upper top quadrant)
- Overall in good shape
  
- What studies to perform??
- TNM staging

# Mammography

- Screening and diagnostic tool for breast cancer
- Very sensitive and specific for breast cancer
- Cheap
  
- Measuring of primary tumor (in mm)
  - T stage
- Diagnosis of local lymphatic nodes
  - N stage
  
- Sometimes accompanied by ultrasound or breast MRI



# Breast cancer staging

T classification	Tumor size, characteristic
T0	No evidence of primary tumor.
T1	Tumor $\leq 20$ mm in greatest dimension.
T1a	Tumor $> 1$ mm but $\leq 5$ mm in greatest dimension.
T1b	Tumor $> 5$ mm but $\leq 10$ mm in greatest dimension.
T1c	Tumor $> 10$ mm but $\leq 20$ mm in greatest dimension.
T2	Tumor $> 20$ mm but $\leq 50$ mm in greatest dimension.
T3	Tumor $> 50$ mm in greatest dimension.
T4	Tumor of any size with direct extension to the chest wall and/or to the skin (ulceration or skin nodules)
T4a	Extension to the chest wall, not including only pectoralis muscle adherence/invasion.
T4b	Ulceration and/or edema (including peau d'orange) of the skin, which do not meet the criteria for inflammatory carcinoma.
T4c	Both T4a and T4b.
T4d	Inflammatory carcinoma.

# Looking for distant metastases

- M stage
- Performing studies for:
  - Chest: X-ray, CT scan
  - Abdomen and pelvis: ultrasound, CT scans
  - Whole body – PET or PET/CT, wb CT
  - Bones – scintigraphy
  - Brain – MRI or CT

# Breast cancer staging

Stage	T	N	M
I	T1	N0	M0
IIA	T0	N1	M0
	T1	N1	M0
	T2	N0	M0
IIB	T2	N1	M0
	T3	N0	M0
IIIA	T1-3	N2	M0
	T3	N1	M0
IIIB	T4	Any N	M0
IIIC	Any T	N3	M0
IV	Any T	Any N	M1

Stage	5-year Survival Rate
I	95%
IIA	85%
IIB	80%
IIIA	67%
IIIB	41%
IIIC	49%
IV	15%

# Case 1

- 62 years old
- Left breast cancer 22mm - T2
- 2 pathologic lymphatic nodes in left axila – N1
- No distant metastases – M0
  
- TNM: T2 N1 M0
- Stage IIB
  
- What is next?



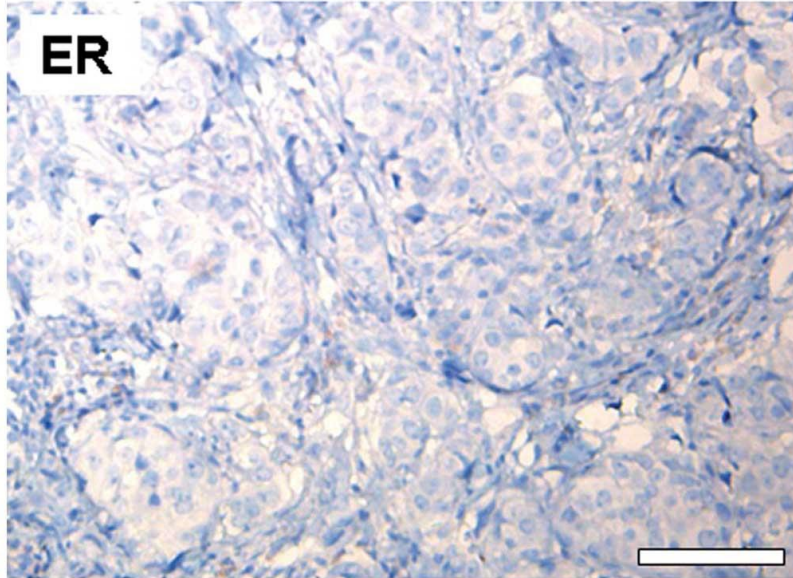
# **Histology**

**what are we dealing with??**

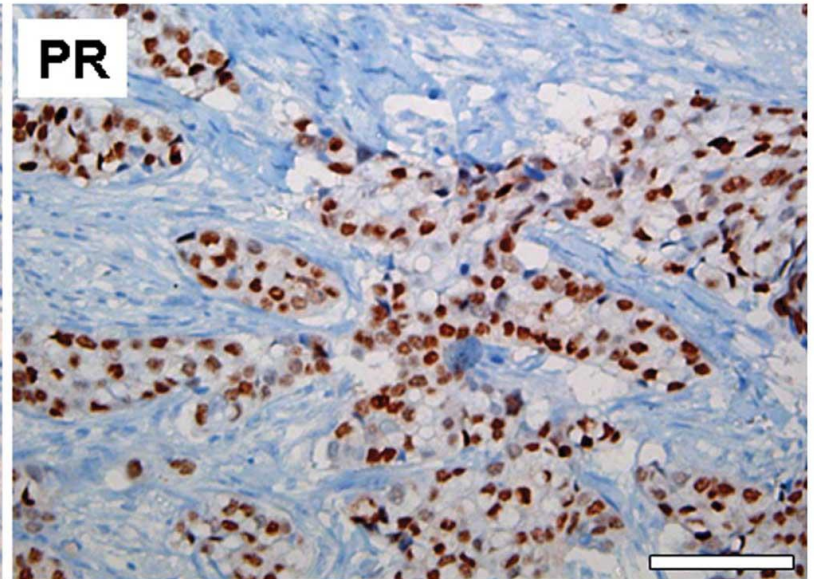
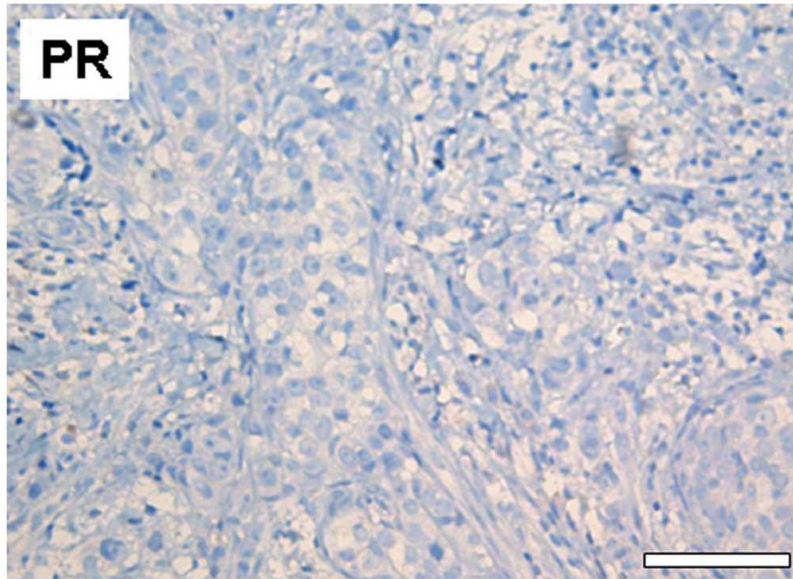
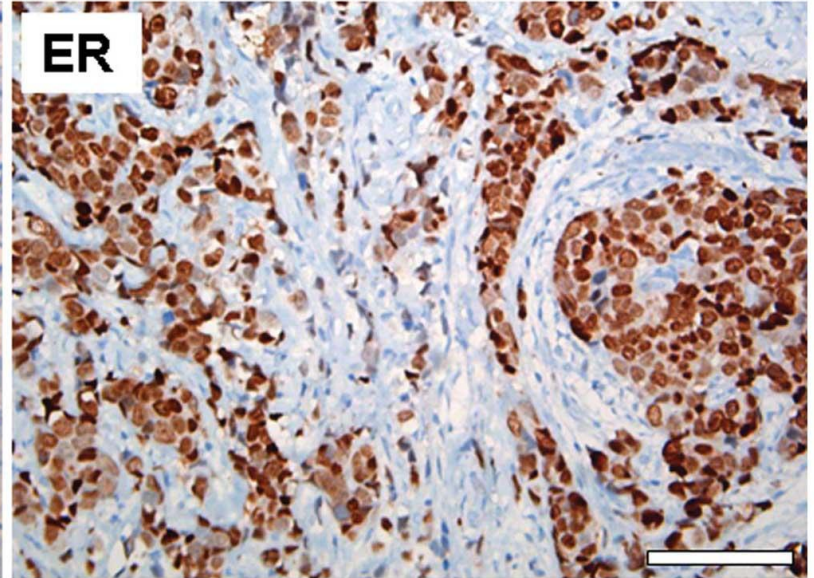
# Histology

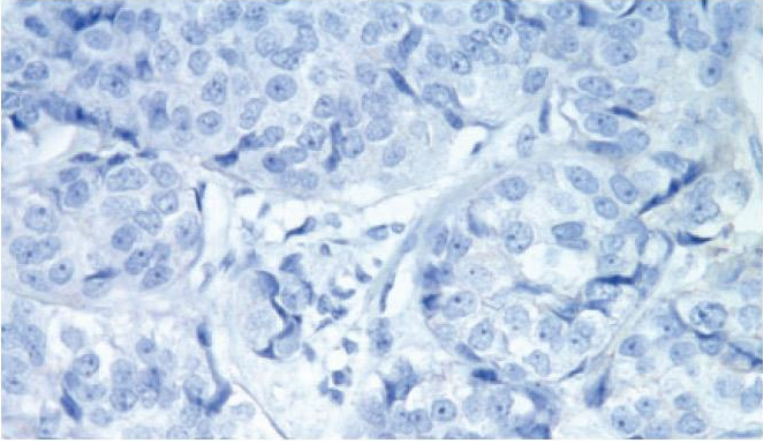
- **Morphology:**
  - Ductal (85%), lobular, medullar, mixed
- **Grade of differentiation** – G1(good)-G3(bad)
- **Molecular diagnostics:**
  - Expression of receptors:
    - **Estrogen** receptor - ER
    - **Progesterone** receptor - PR
    - **HER2** receptor
  - **Ki-67** – marker of proliferation

**Negative**

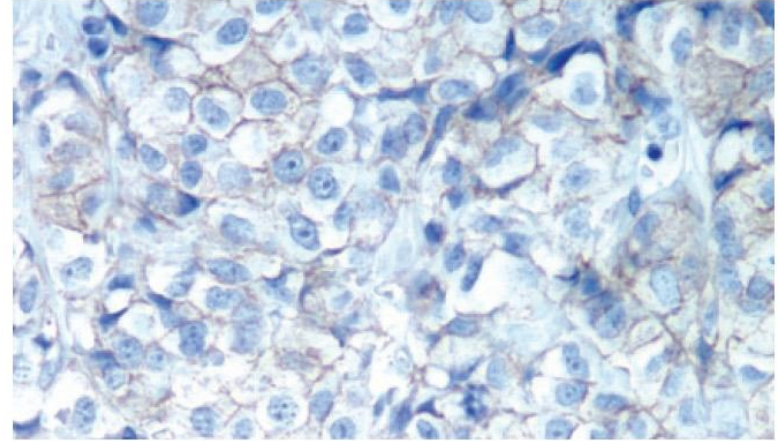


**Positive**

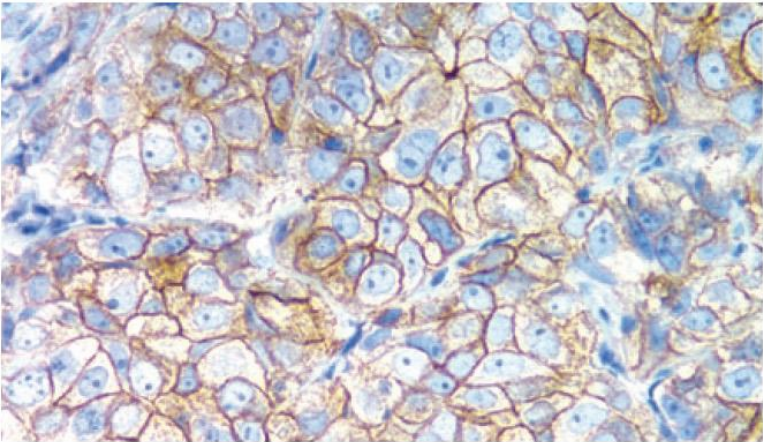




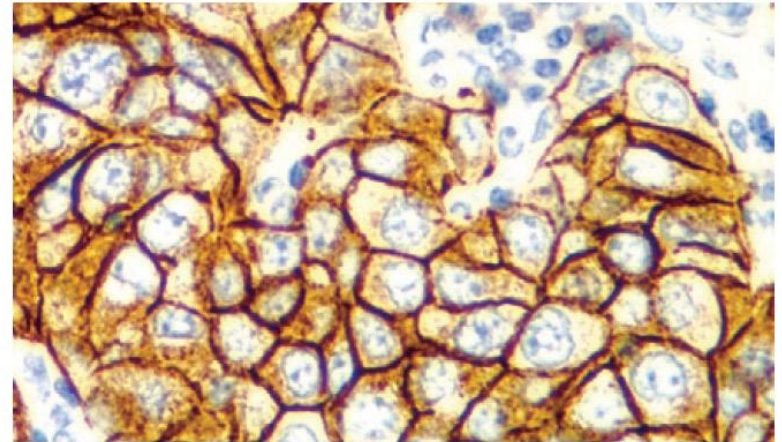
Score: **0** (40x)



Score: **1+** (40x)



Score: **2+** (40x)



Score: **3+** (40x)

# Subtypes of breast cancer

**Luminal A – *less aggressive***

ER+, PR+, HER2-, Ki67 low

**Luminal B**

ER+, PR – or HER2+ or Ki67 high

**Triple negative (10%) *most aggressive***

ER-, PR-, HER2 negative

**HER2 overexpressed (amplified) 15%**

# **Treatment**

**how to cure patient?**

**If not possible, how to prolong the life**

# Principles of cancer treatment

- **In localized tumor – we can cure patients**
  - **Resection** of tumor – only curative modality
  - Sometimes **neoadjuvant** therapy – treatment before surgery – chemotherapy and/or radiotherapy
    - To shrinking the tumor and allow less extensive surgery
  - **Adjuvant** treatment – treatment after surgery
    - To lower the risk of tumor relapse
  - Toxicity is not the main concern (temporary)
- **In metastatic disease – we can prolong life**
  - **Systemic** treatment – chemotherapy, hormonal therapy, targeted therapy
  - Toxicity matter, quality of life is very important

**Surgery**

**until we can get rid of it!!!**



# Mastectomy

- **Total mastectomy** – removal of entire breast



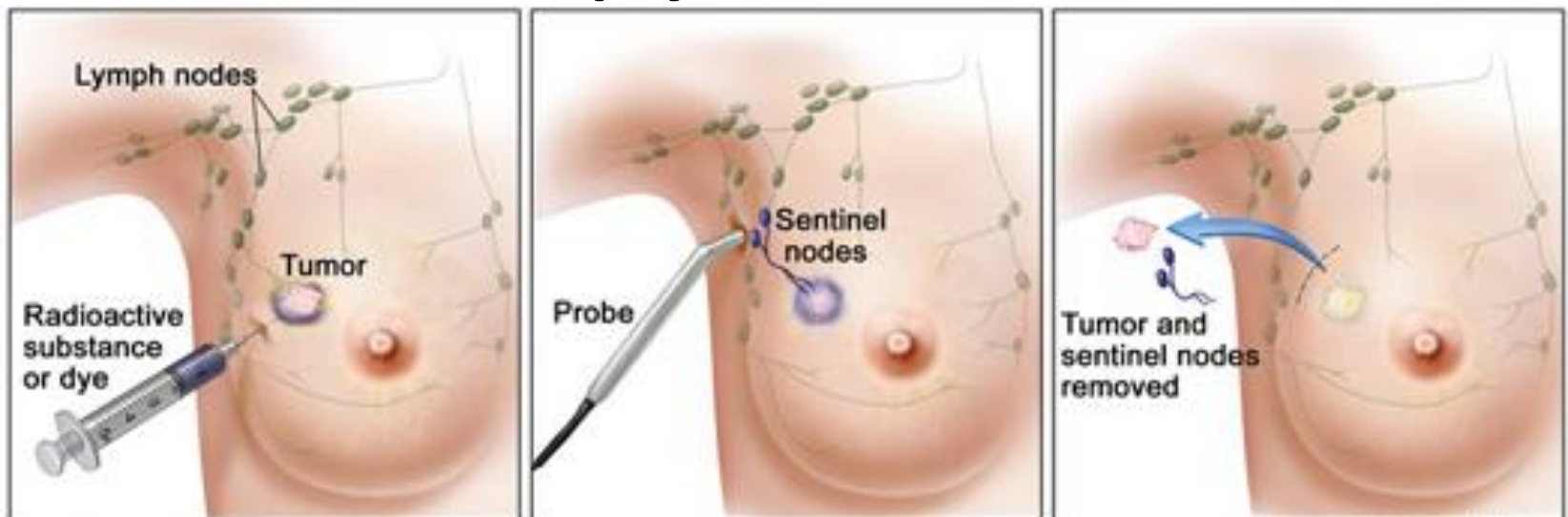
# Partial mastectomy

- Breast-conserving surgery - only removes the part of the breast that has cancer and surrounding tissue
- The aim is to resect as little tissue as possible to keep the breast in its original shape



# Surgery of axilla

- **Axillary lymph node dissection - ALND**
  - incision under the arm and removing 10–40 lymph nodes from level I and level II
  - Procedure in all patients with positive lymph nodes
  - Risk of lymphedema
- **Sentinel nodes biopsy – SNB**



# Adjuvant treatment

go away and never come back!!



# Adjuvant treatment

- Treatment **after** surgery
- Reduce the risk of the cancer to relapse (coming back)
- Multimodal therapy:
  - Chemotherapy – 4-5 months
  - Targeted therapy (in HER2 posit.) – 1 year
  - Radiotherapy – 3-5 weeks
  - Hormonal therapy (in ER/PR posit.) – 5 – 10 years

# Chemotherapy for breast cancer

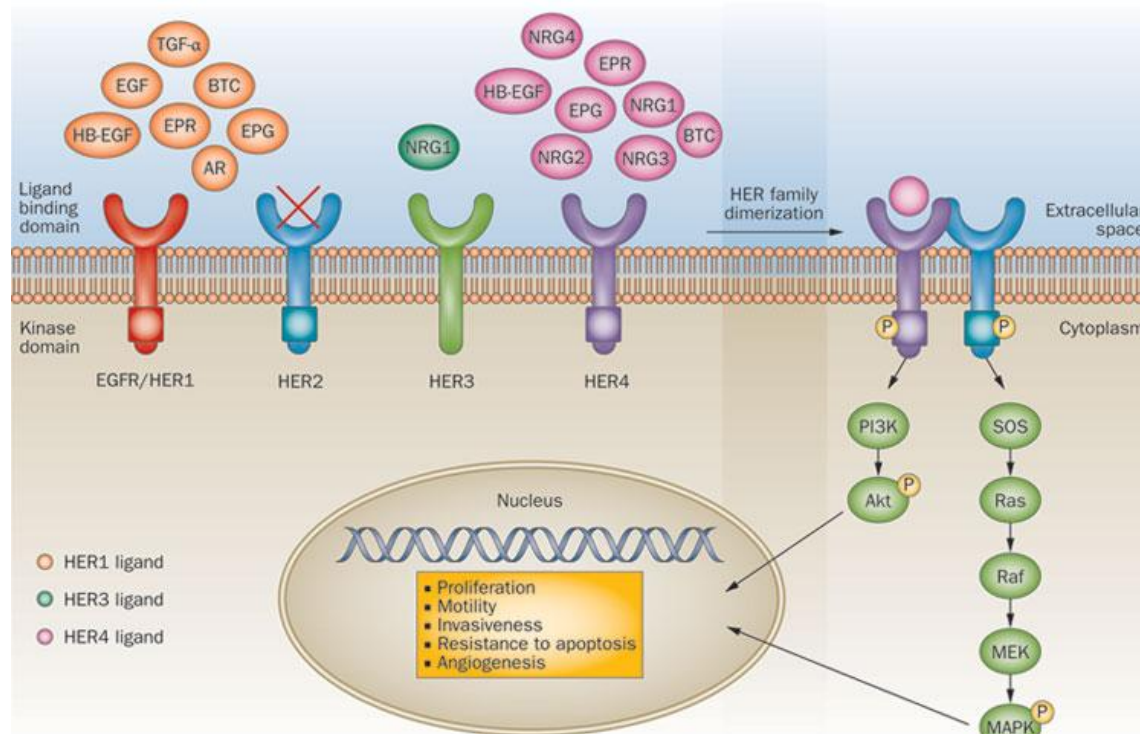
- In selected patients with high risk breast cancer (not all patients need chemo):
  - Large tumor
  - Positive lymph nodes
  - Biological aggressive cancer – triple negative, HER2 positive

# Chemotherapy for breast cancer

- Most used cytostatics:
  - **Antracyclines - Doxorubicin, Epirubicin**
  - **Taxanes - Paclitaxel, Docetaxel**
  - Capecitabin
  - Vinorelbin
- Combination in adjuvant treatment:
  - AC – doxorubicin+cyklofosamid
  - AC a followed by paclitaxel
  - FAC – flurouracil+doxorubicin+cyklofosamid
  - FEC – flurouracil+epirubicin+cyklofosamid
  - TAC – docetaxel+doxorubicin+cyklofosamid
  - CMF – cyklofosamid+metotrexát+flurouracil
- In palliative settings:
  - Mostly **monotherapy** – paclitaxel, epirubicin, vinorelbin, capecitabin

# Targeted therapy

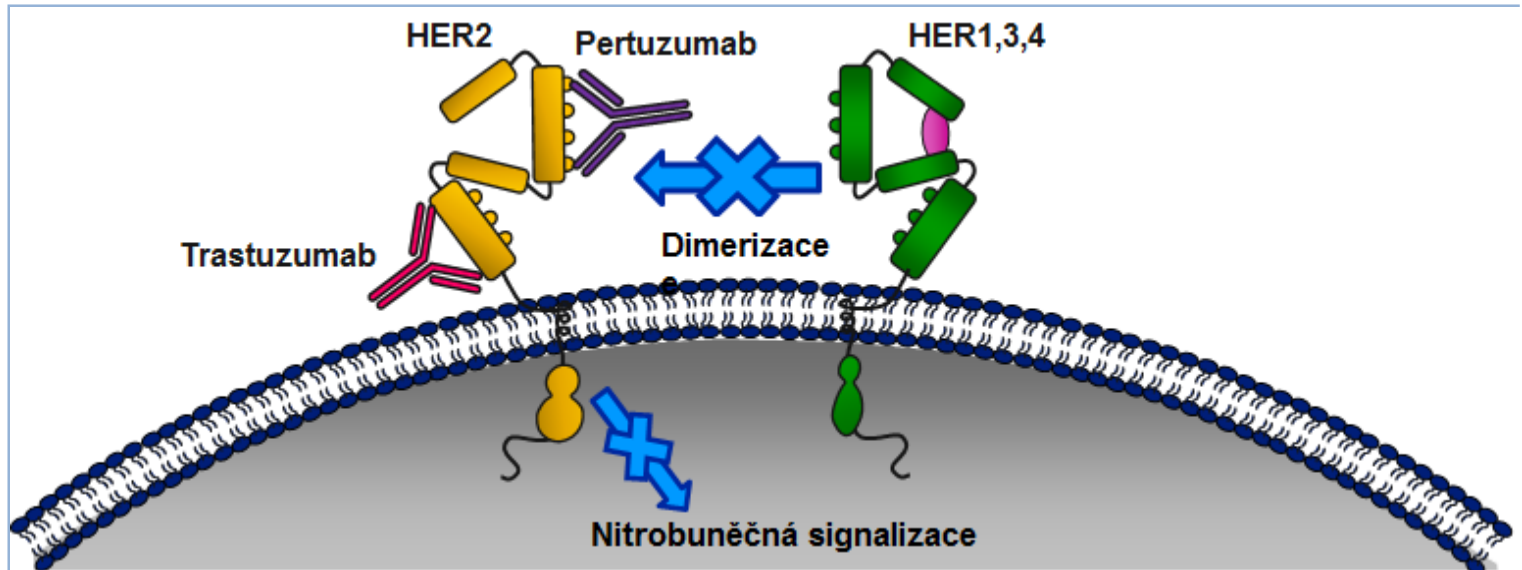
- In HER2 positive breast cancer, about 15% of breast cancer
- HER2 – transmembrane receptor, HER family
- Activation leads to cell survival, metastasis, and resistance to therapy





# HER2 positive breast cancer

- Anti-HER2 treatment – **monoclonal** antibodies against the HER2 receptor
- First used antibody was **trastuzumab** (Herceptine)
- Next generation – **pertuzumab, T-DM1**
- Adding to chemotherapy boosts treatment efficacy



# Hormonal therapy

- About **70% of breast** cancer are hormonal receptor positive (Estrogen or Progesterone receptor) – i.e. **hormonal sensitive disease**
- Low or moderately aggressive disease (Luminal A or B)
- Sensitive to hormonal therapy:
  - **Tamoxifen** (Selective Estrogen Receptor Modulator - SERM)
  - **Aromatase inhibitors**
    - Non-steroidal AI (anastrozole, letrozole)
    - Steroidal (exemestan)
  - **direct ER inhibitor** (fulvestrant)

# Hormonal therapy

- In adjuvant setting **used for 5-10 years**
- Very effective in **Luminal A** breast cancer subtype
- Many patients can omit chemotherapy and use only hormonal therapy
- **Very good toxicity profile** (hot flashes, bone or joint pain, arteficial menopause, *endometrial carcinoma in tamoxifen*)

# Radiotherapy

- **After** surgery and chemotherapy
- **Always after partial mastectomy**, sometimes after total mastectomy (large tumor, positive lymph nodes)
- Duration 3-5 weeks, dose 50 Gy
- Reduce local recurrence of cancer but also prolongs survival
- Adverse events: post radiation dermatitis, skin desquamation

# Radiotherapy



# **Oncological treatment of an advanced incurable disease**

**prolong life**  
and  
**improve QoL**

# Treatment in metastatic setting

- In ER/PR positive breast cancer (Luminal A/B subtype) is **hormonal therapy** very effective
  - Tamoxifen → Aromatase Inhibitors → Fulvestrant
- If hormonal therapy does not work anymore or in ER/PR negative disease – **chemotherapy**
  - First line, second line, third line....
- In HER2 positive disease combination with **targeted therapy** (trastuzumab, pertuzumab, T-DM1)

# Chemotherapy

- Usually using in monotherapy
- If one chemotherapy does not work, choose another (another line), etc.
- Anthracyclines:
  - Doxorubicin
  - Epirubicin
  - liposomal doxorubicin
- Taxanes
  - Paclitaxel
  - Docetaxel
  - Nab-paclitaxel
- Vinca alkaloids
  - Vinorelbin
- Antimetabolites
  - Capecitabine
  - Gemcitabine
  - Fluorouracil
- Platin derivatives
  - Carboplatin
  - Cisplatin
- Other cytostatics
  - Cyclophosphamide
  - Methotrexate
  - Eribuline



# Specific treatment

- In bone metastases – bone-modifying agents (BMA) – bisphosphonates, denosumabu
- In painful bone metastases – radiotherapy
- In central nervous system metastases - radiotherapy
- In pleural effusion – drainage
- Social, psychosocial, spiritual support

# Summary

- Breast cancer is a common diagnosis
- Heterogeneous diseases - various biological subtypes
- Therapy is complex - multimodal - surgery, chemotherapy, hormonal therapy, targeted therapy, radiotherapy...
- + supportive treatment !!!

Thank you  
for your  
attention

