

Uncertainty in Medical Imaging

It's all over the chain!

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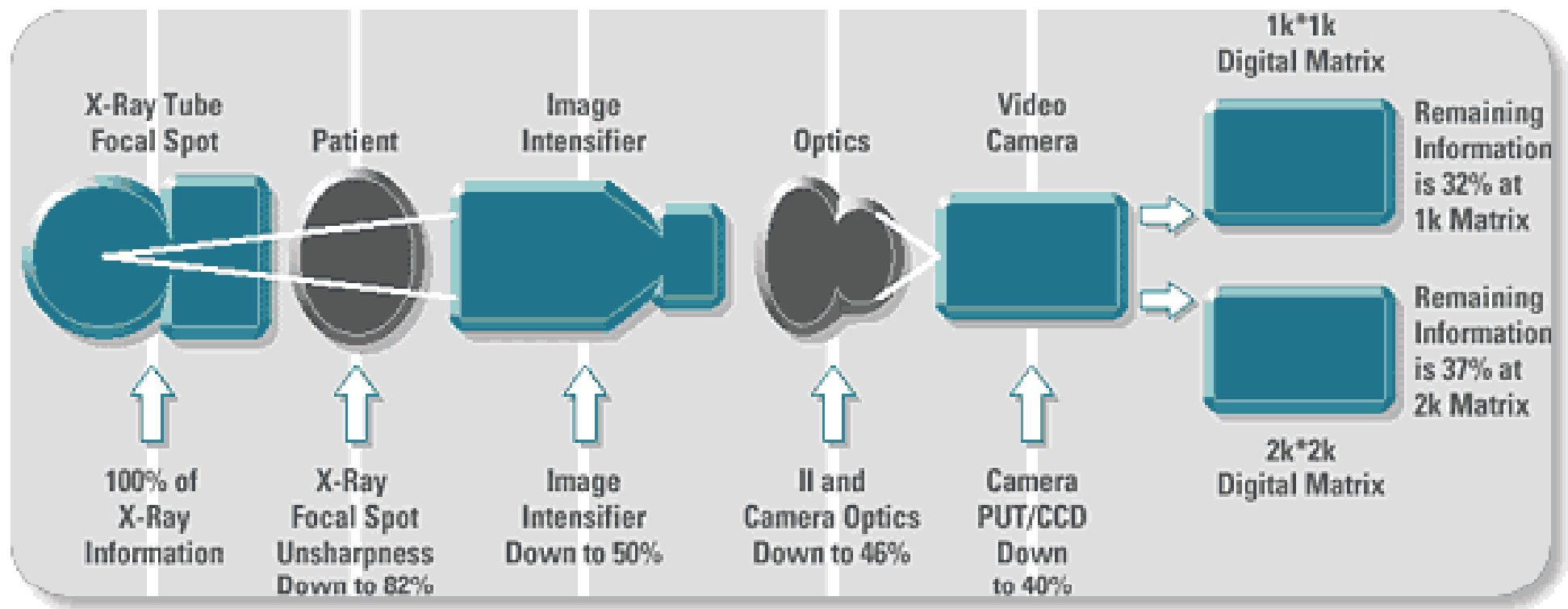
LRCB – Dutch Reference Centre for Screening

Nijmegen, the Netherlands

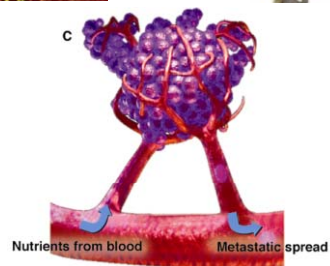
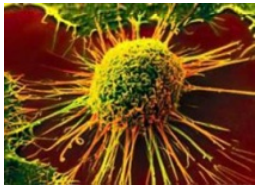


Radboudumc

The old imaging chain...



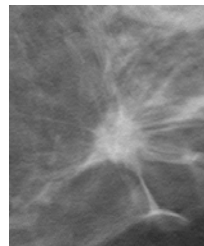
...but today, the longer chain



Biology



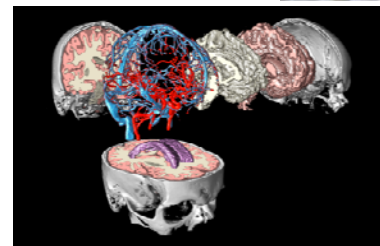
Physics



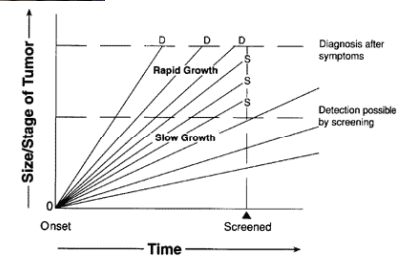
Engineering



Perception

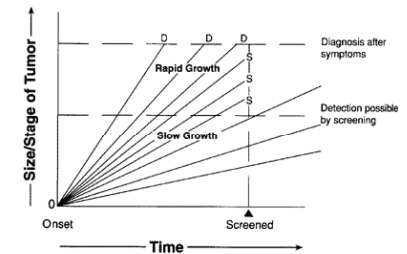
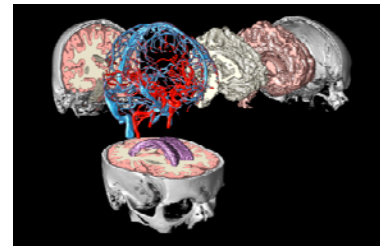
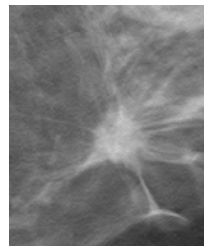
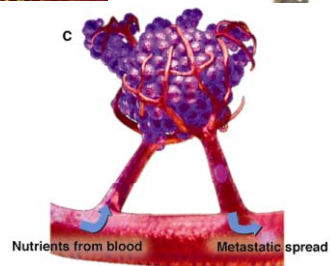
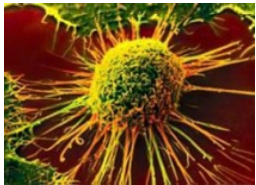


Mathematics



Epidemiology

...but today, the longer chain



Biology

Physics

Tomorrow!

Engineering

Mathematics

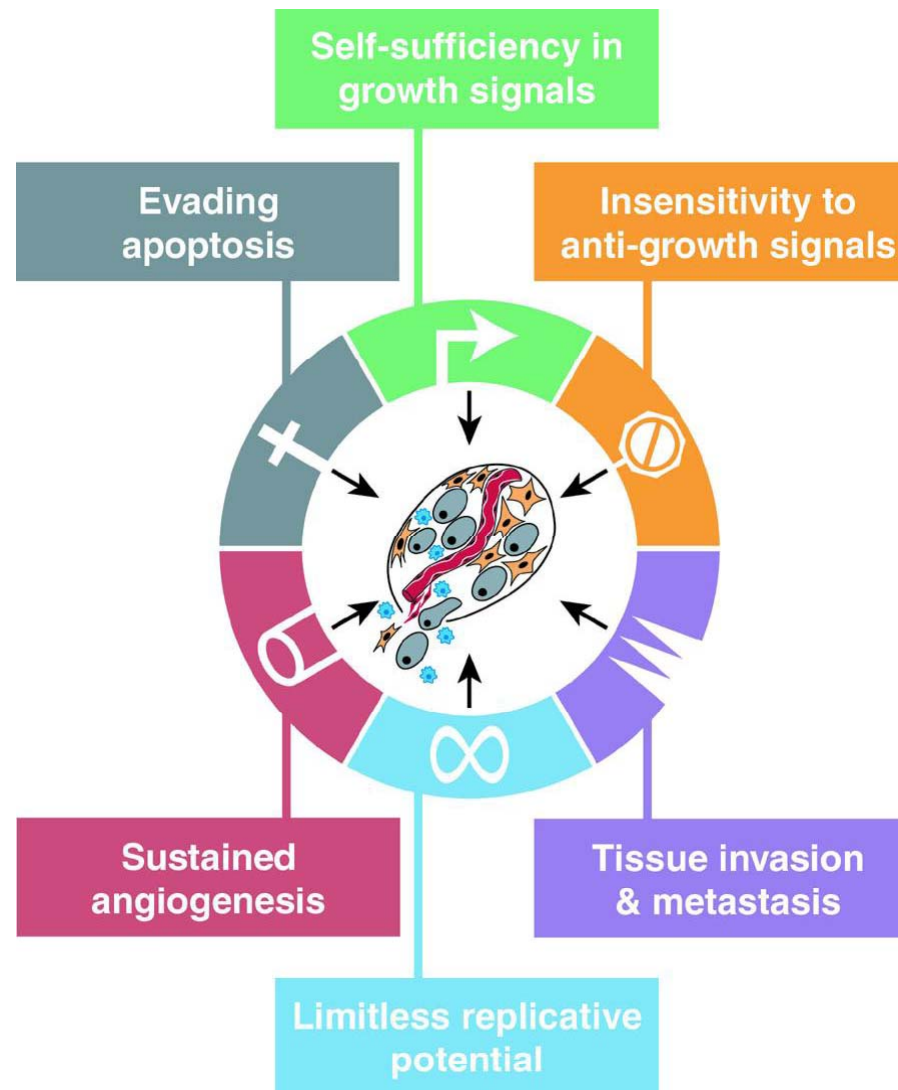
Other talks...

Perception

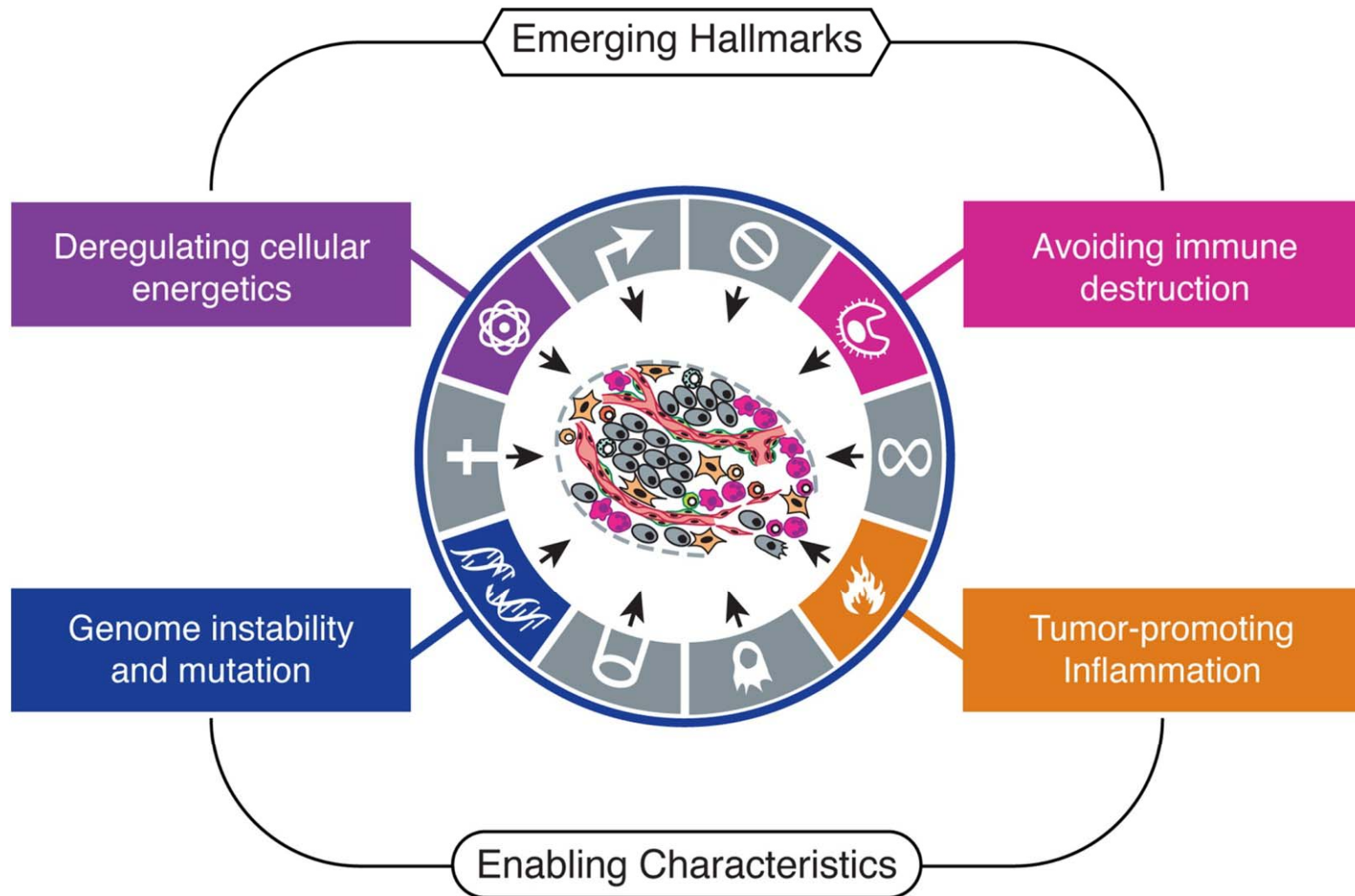
Epidemiology

UNCERTAINTY: BIOLOGY

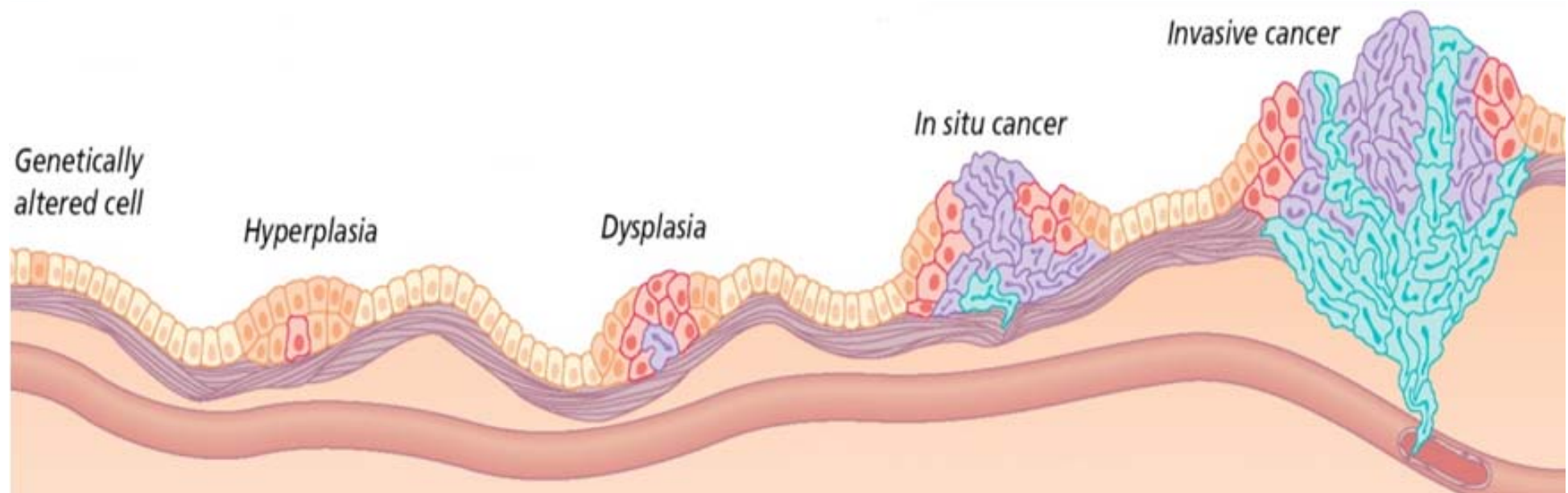
What is cancer?



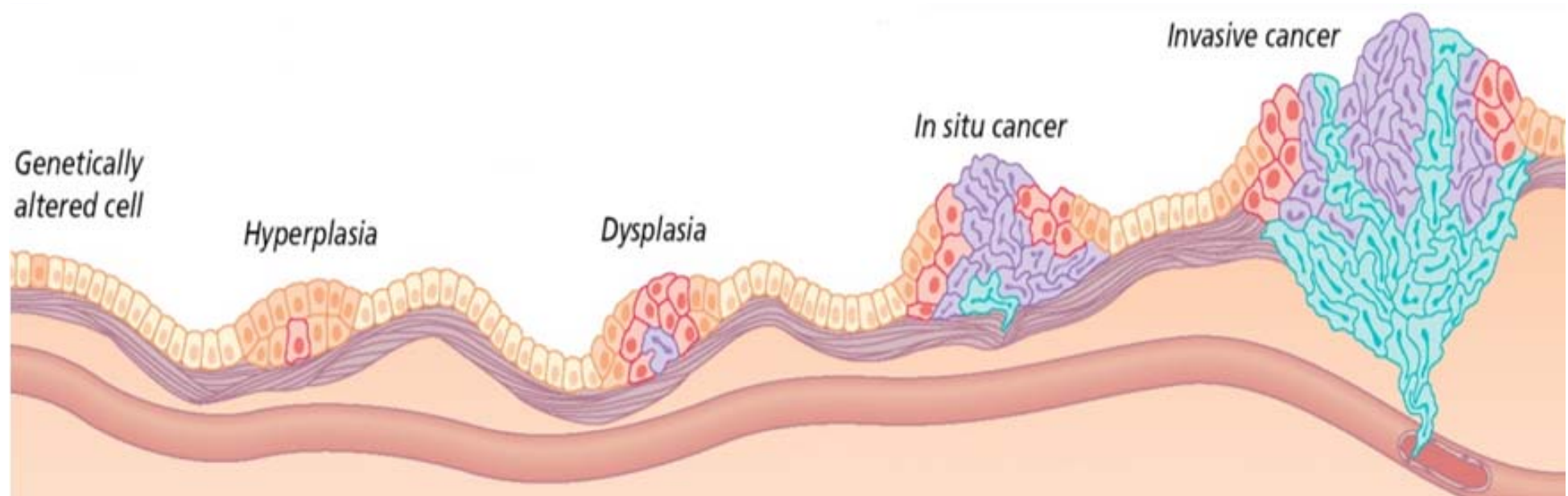
What is cancer?



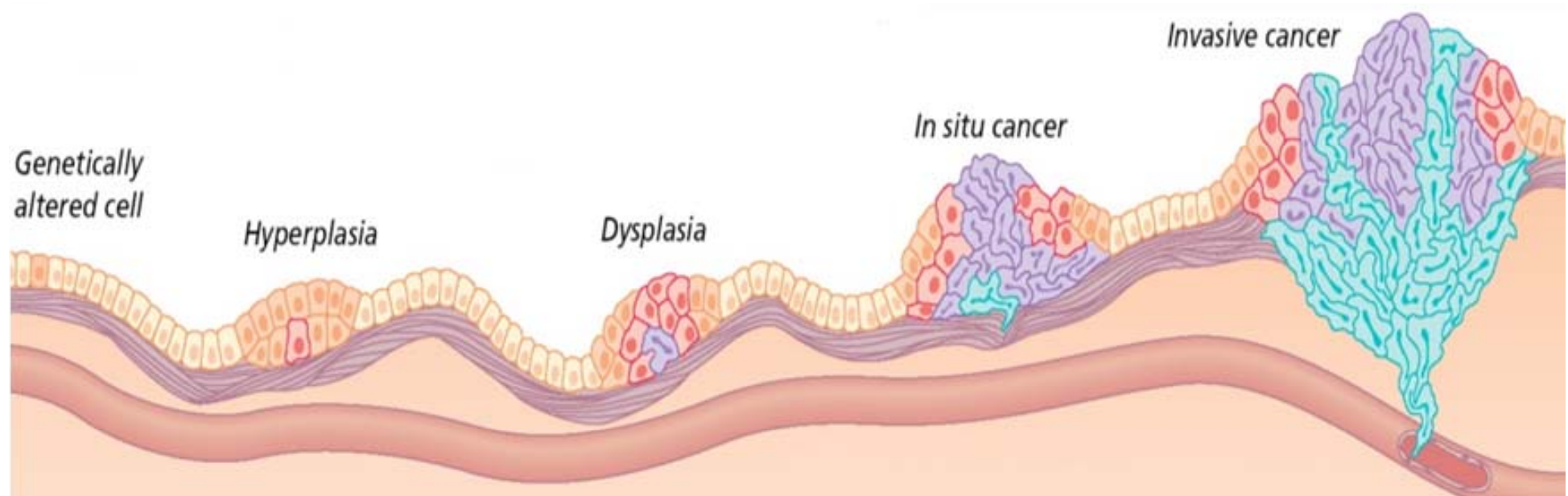
Tumor development



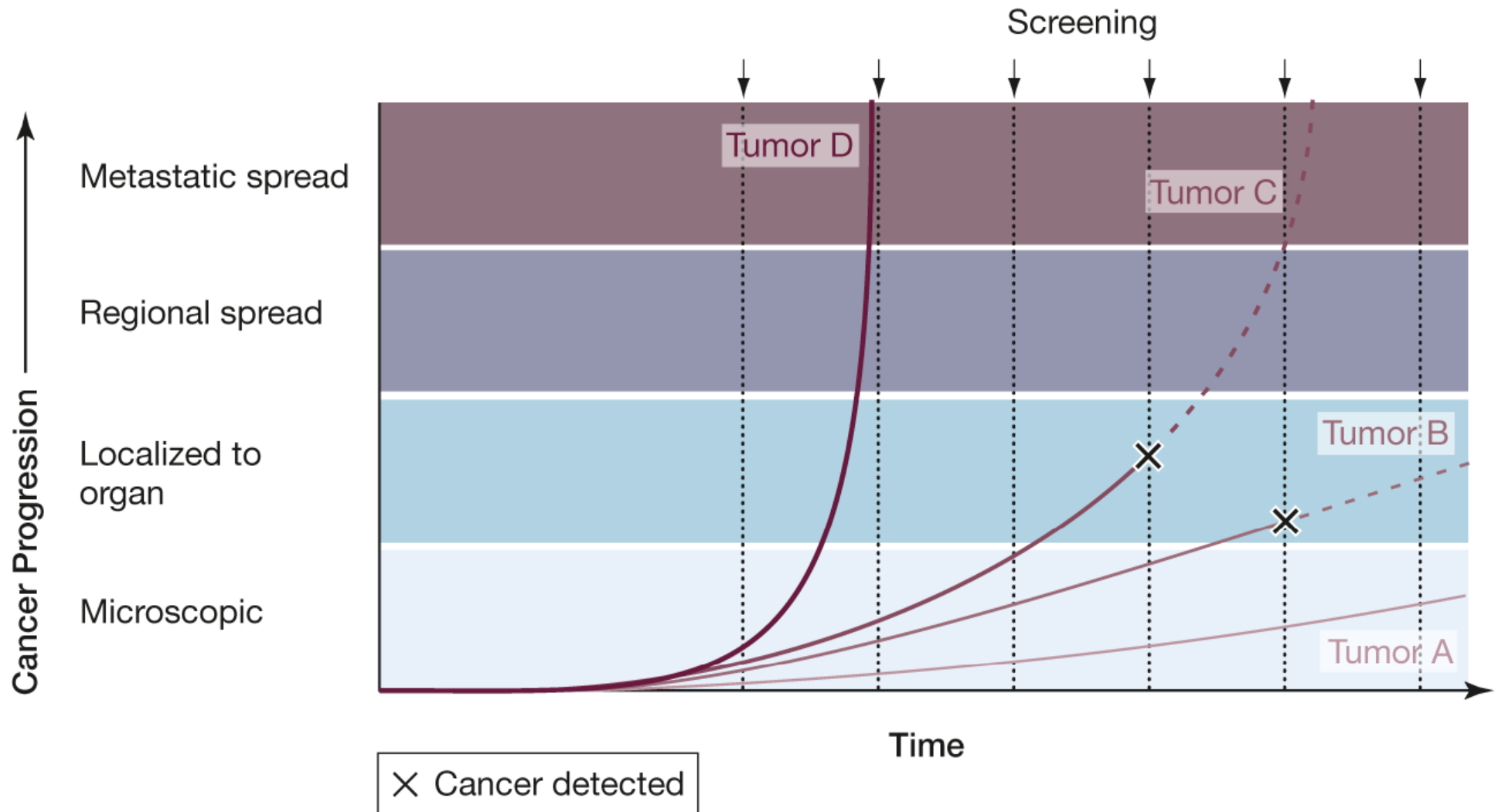
When should we detect cancer?



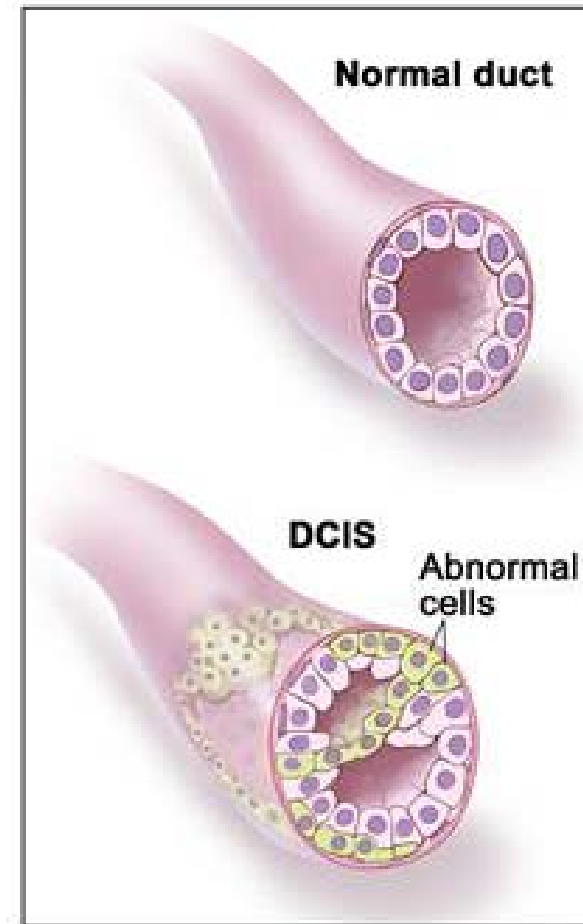
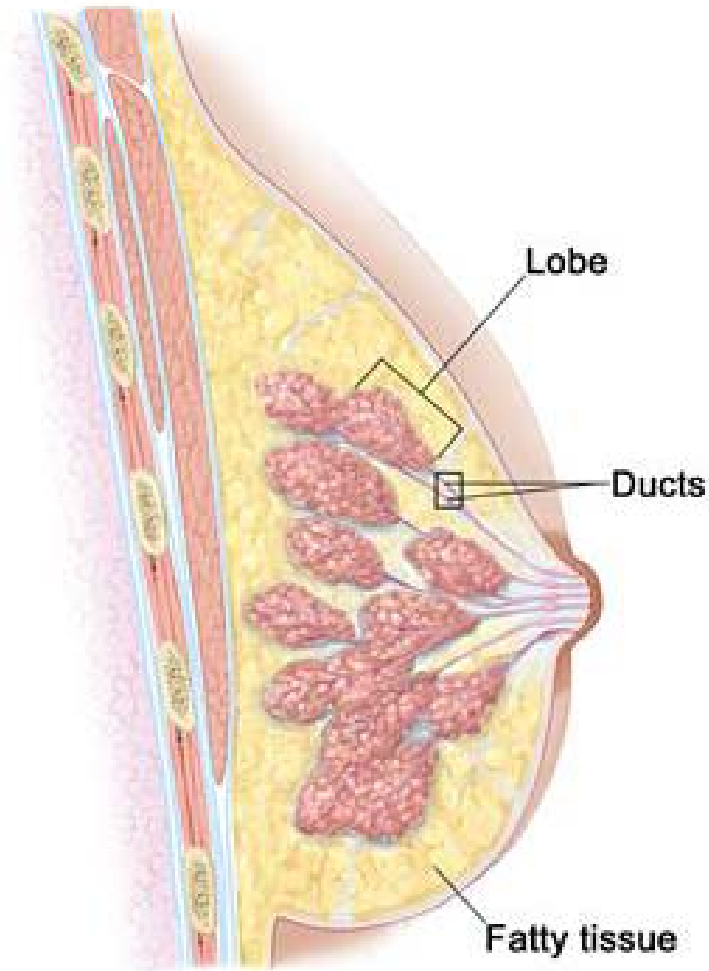
When should we TREAT cancer?



Disease growth and detection



Ductal Carcinoma In Situ (DCIS)



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In situ cancers reported separately

	Detected DBT total	Detected DBT alone	Detected DM total	Detected DM alone
Total	67	21	47	1
Total invasive cancers	58	17	41	-
Total in situ cancers	9	4	6	1

Over-detection?

Imaging

Physical exam

Genetic testing

Over-diagnosis?

Pathology

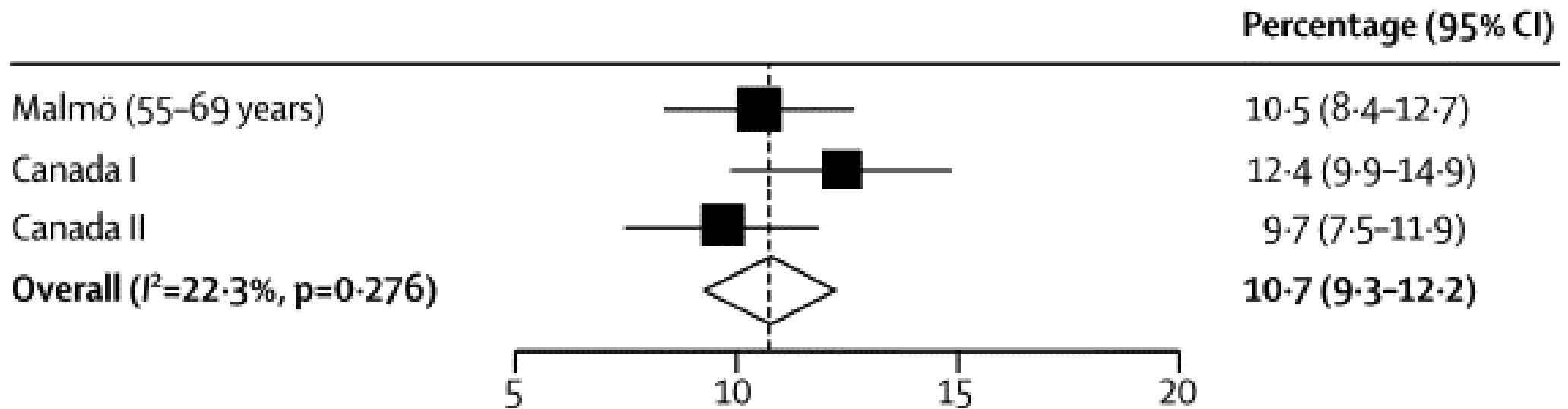
Over-treatment?

Lumpectomy or
Mastectomy
Radiotherapy
Chemotherapy

Co-morbidities

Death due to	HR
Other coronary heart diseases	1.14
Heart failure	1.29
Other heart disease	1.24
Gastrointestinal disease	1.1
External causes	1.14
Suicide	1.39
Symptoms	1.09
Diabetes	1.18
Pulmonary circulation	1.51
Urinary system disease	1.16
Other bacterial disease	1.2

Estimating over-diagnosis

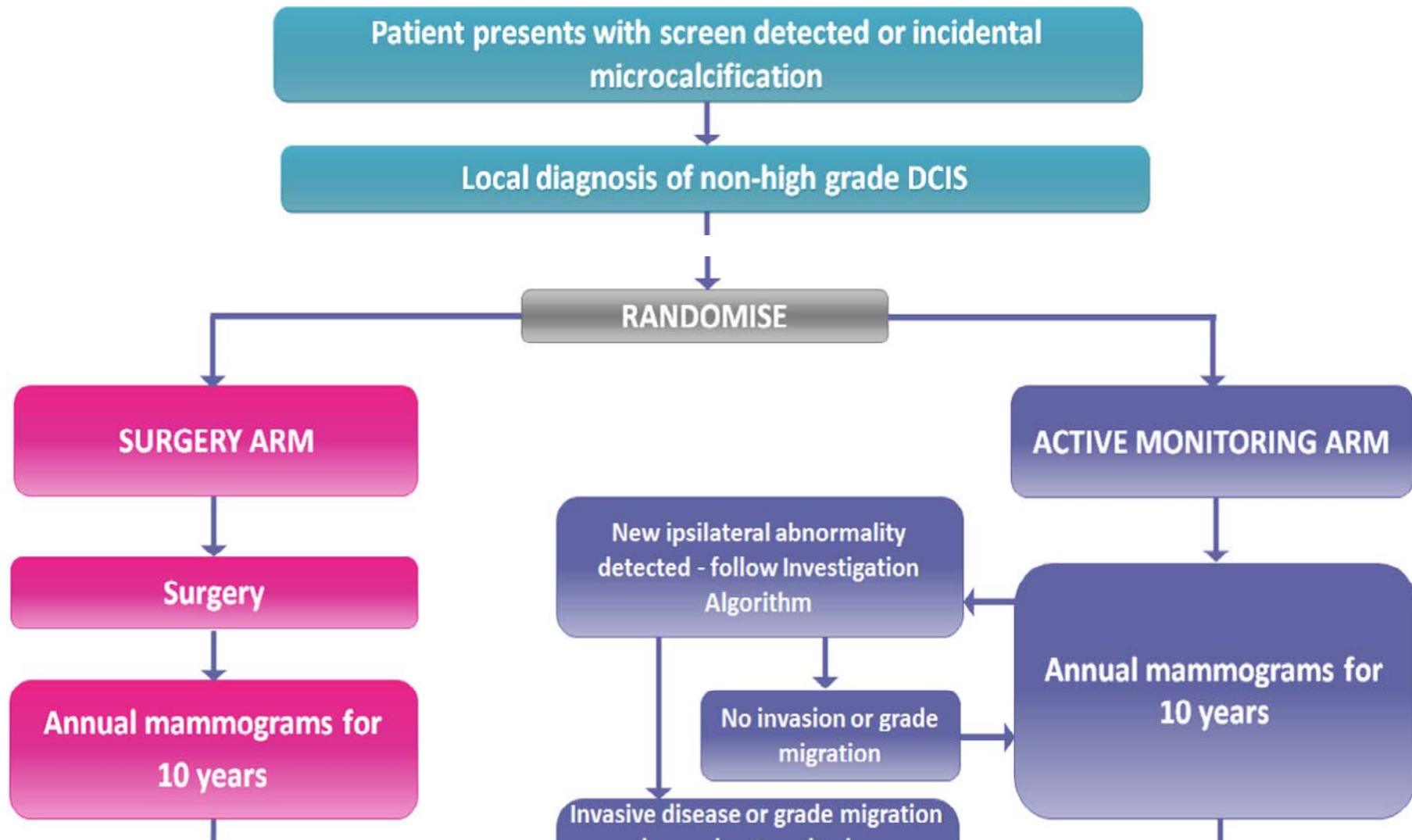


To be continued...

So don't over-treat...

Which ones?

The LORIS trial: 932 patients



The LORD trial

1240 women aged

≥ 45 years

asymptomatic, screen-detected,

pure low-grade DCIS

microcalcifications only.

The LORD trial

Standard treatment + annual mammo
vs.

Annual mammo only

Primary end-point: 10-year ipsilateral
invasive breast cancer free
percentage

UNCERTAINTY: Biology

Different types and
stages of (breast)
cancer

UNCERTAINTY: Biology

Some tumors will never
kill you

UNCERTAINTY: Biology

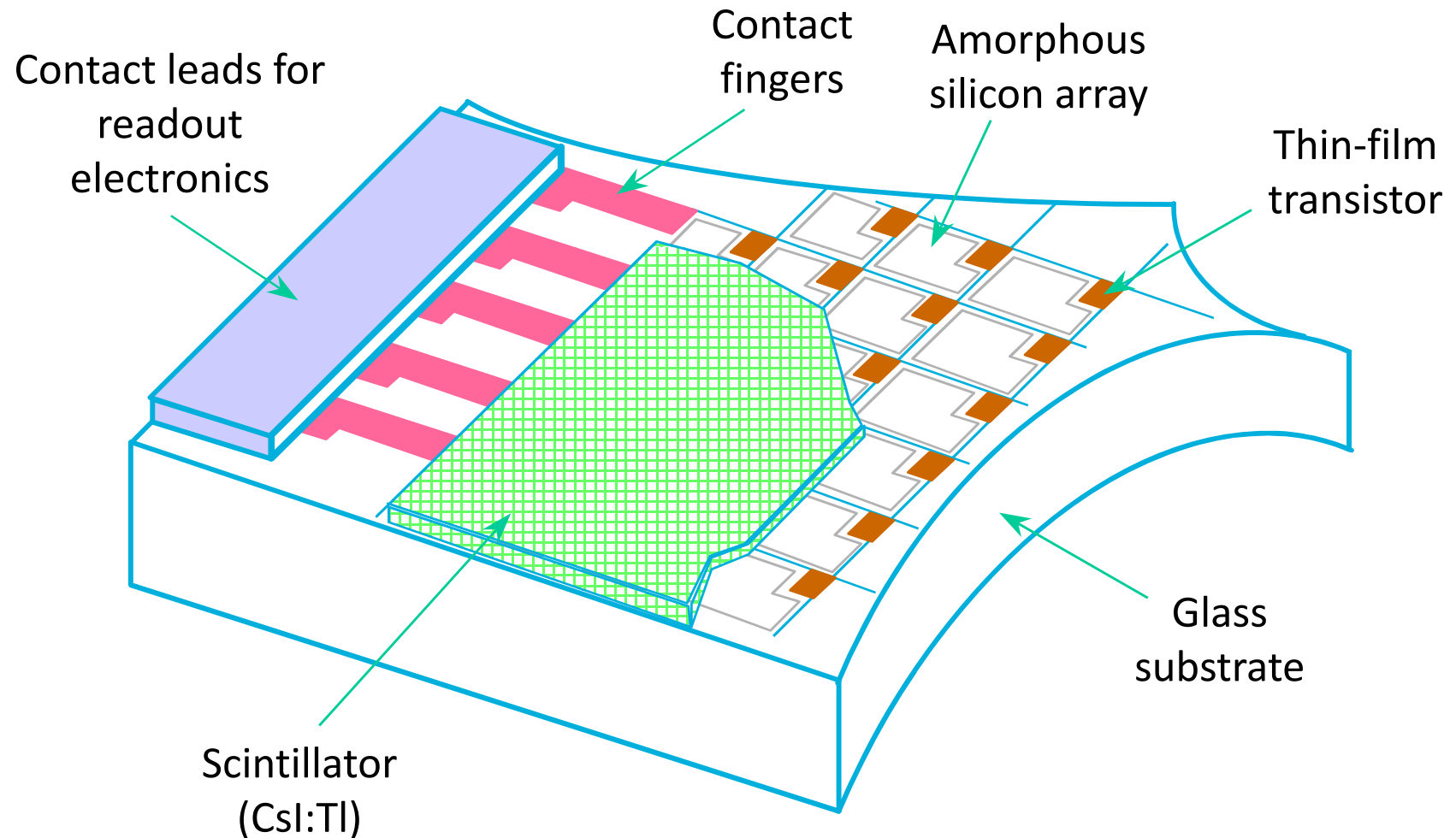
Need to discriminate
which ones

UNCERTAINTY: Biology

How should they be
dealt with?

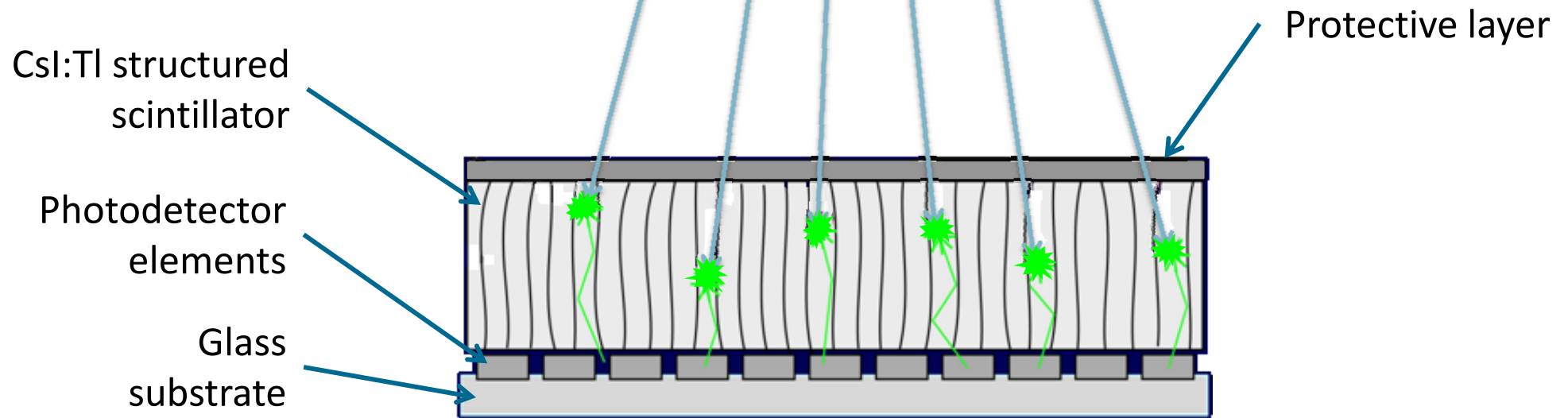
UNCERTAINTY: ENGINEERING

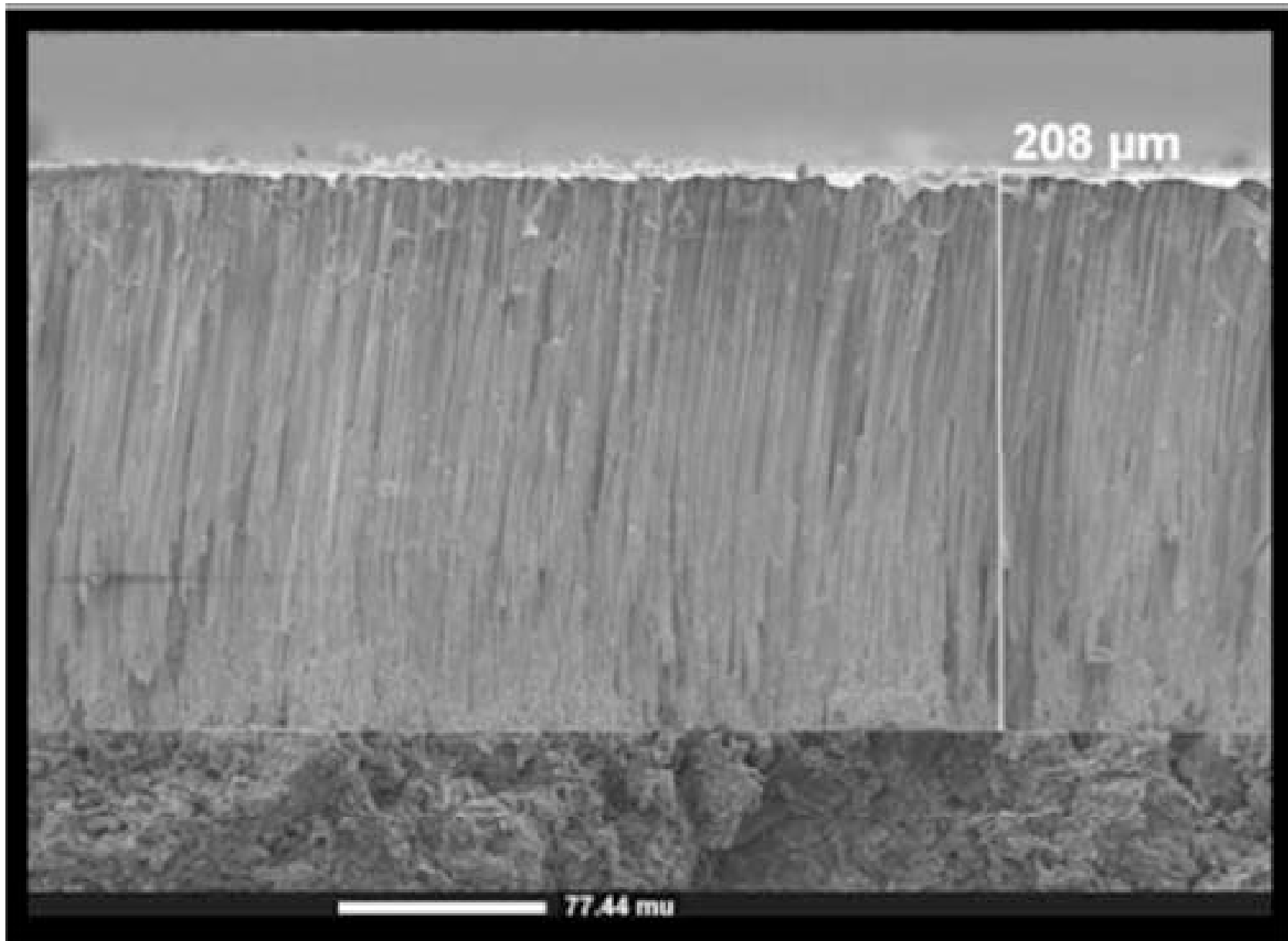
Indirect digital detector

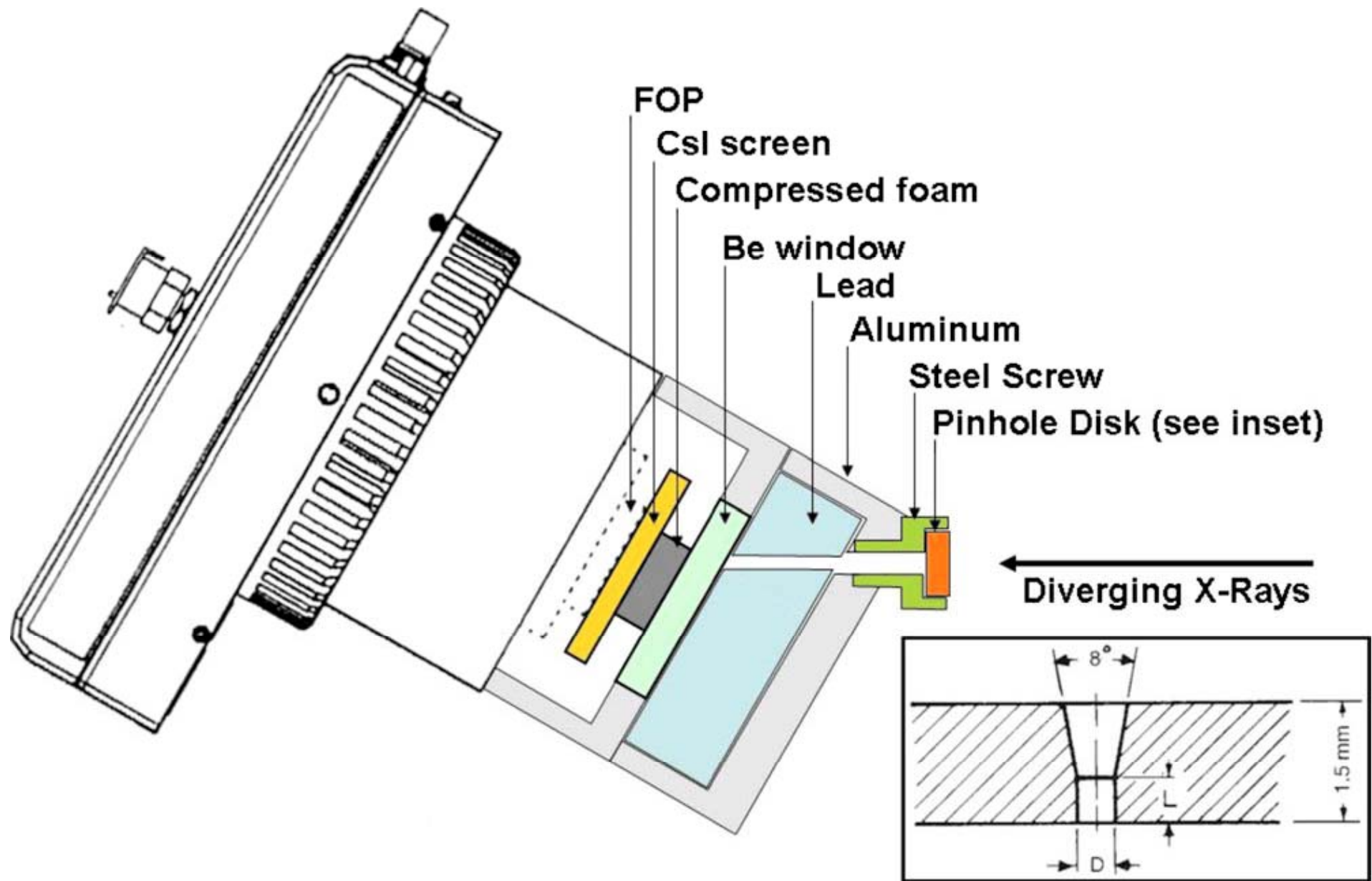


Indirect digital detector

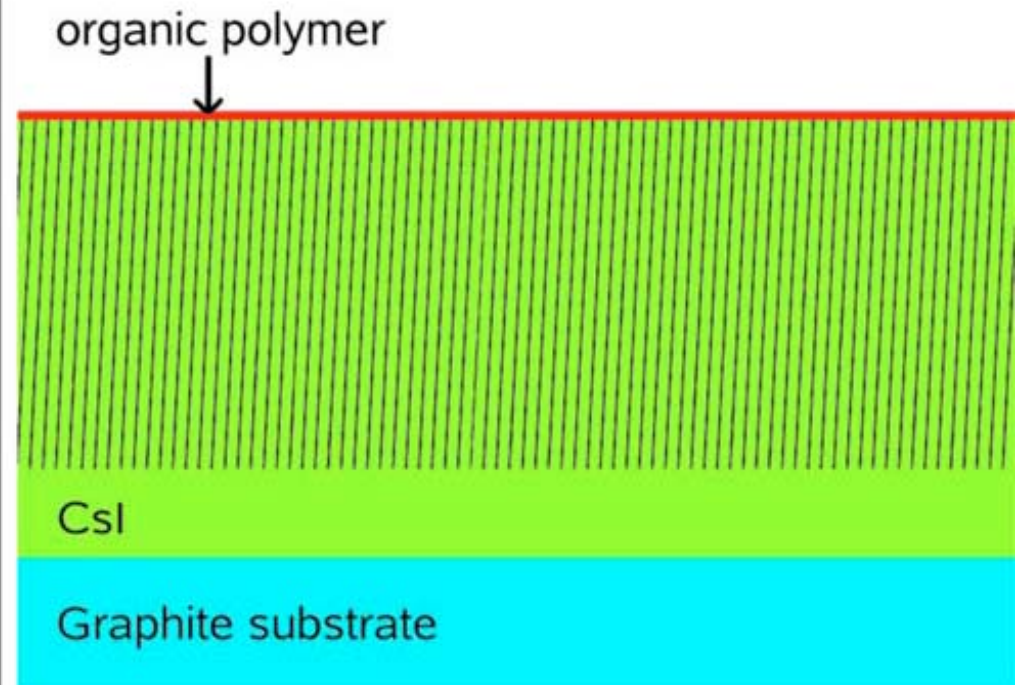
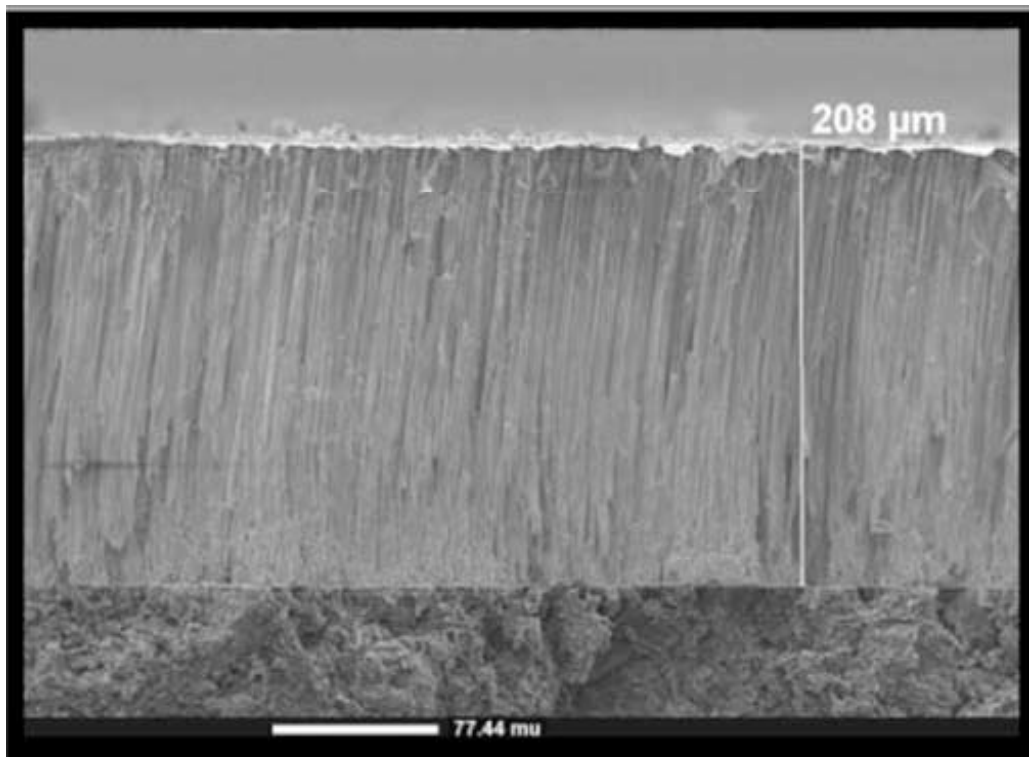
X-rays



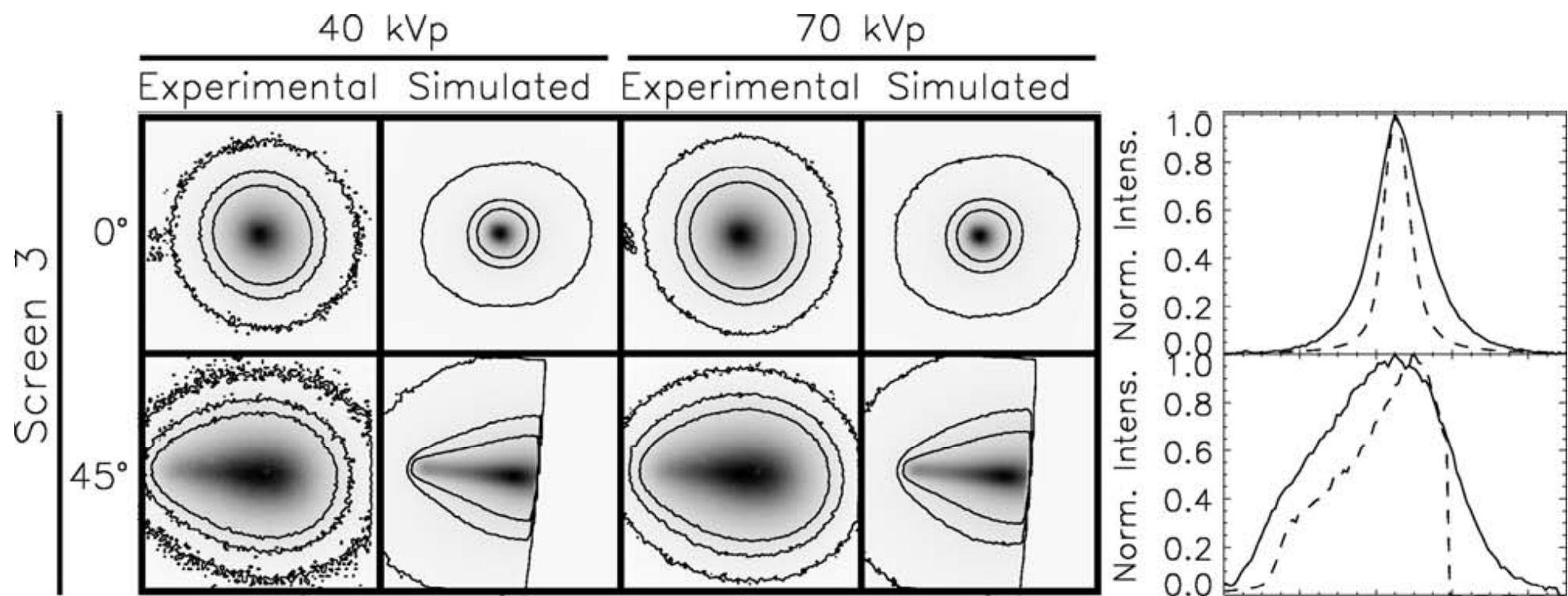




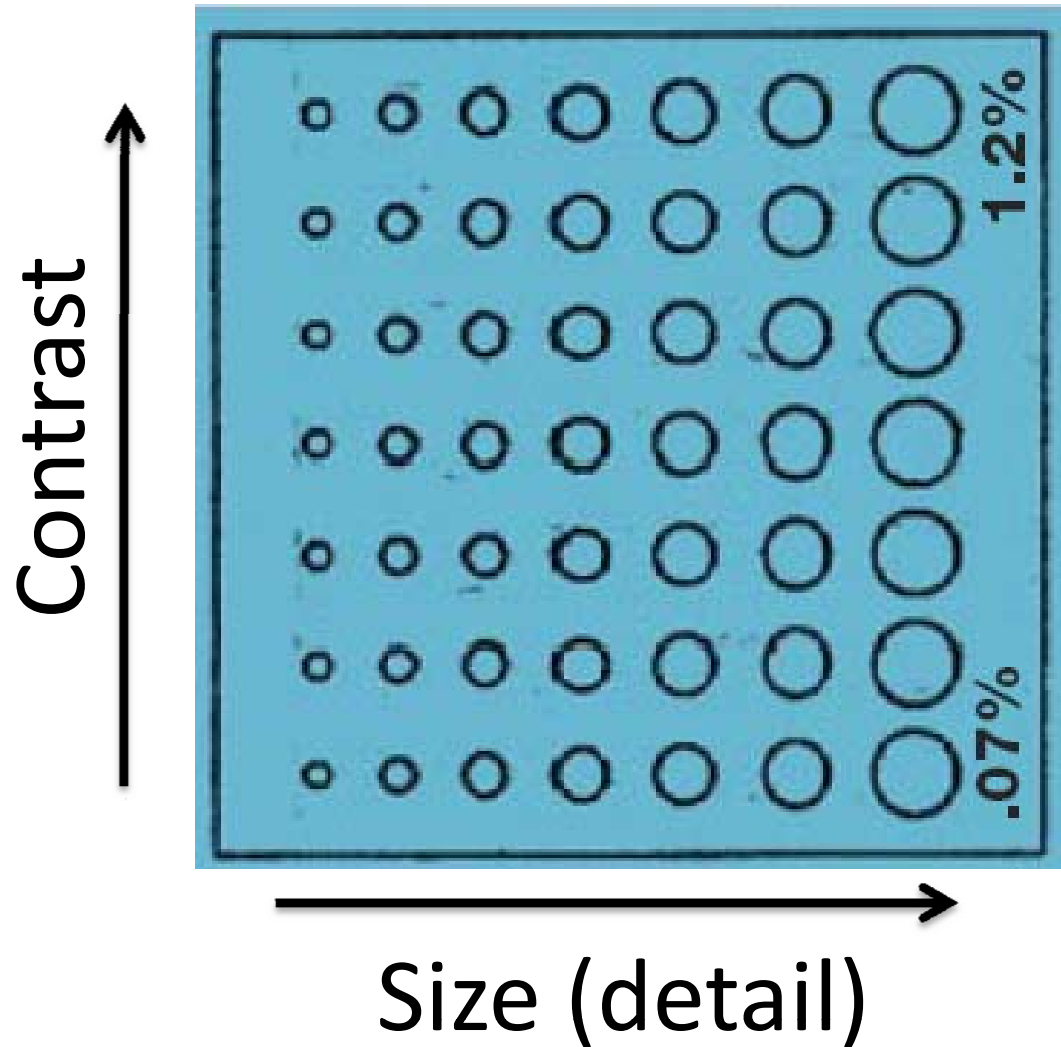
How do you simulate that?



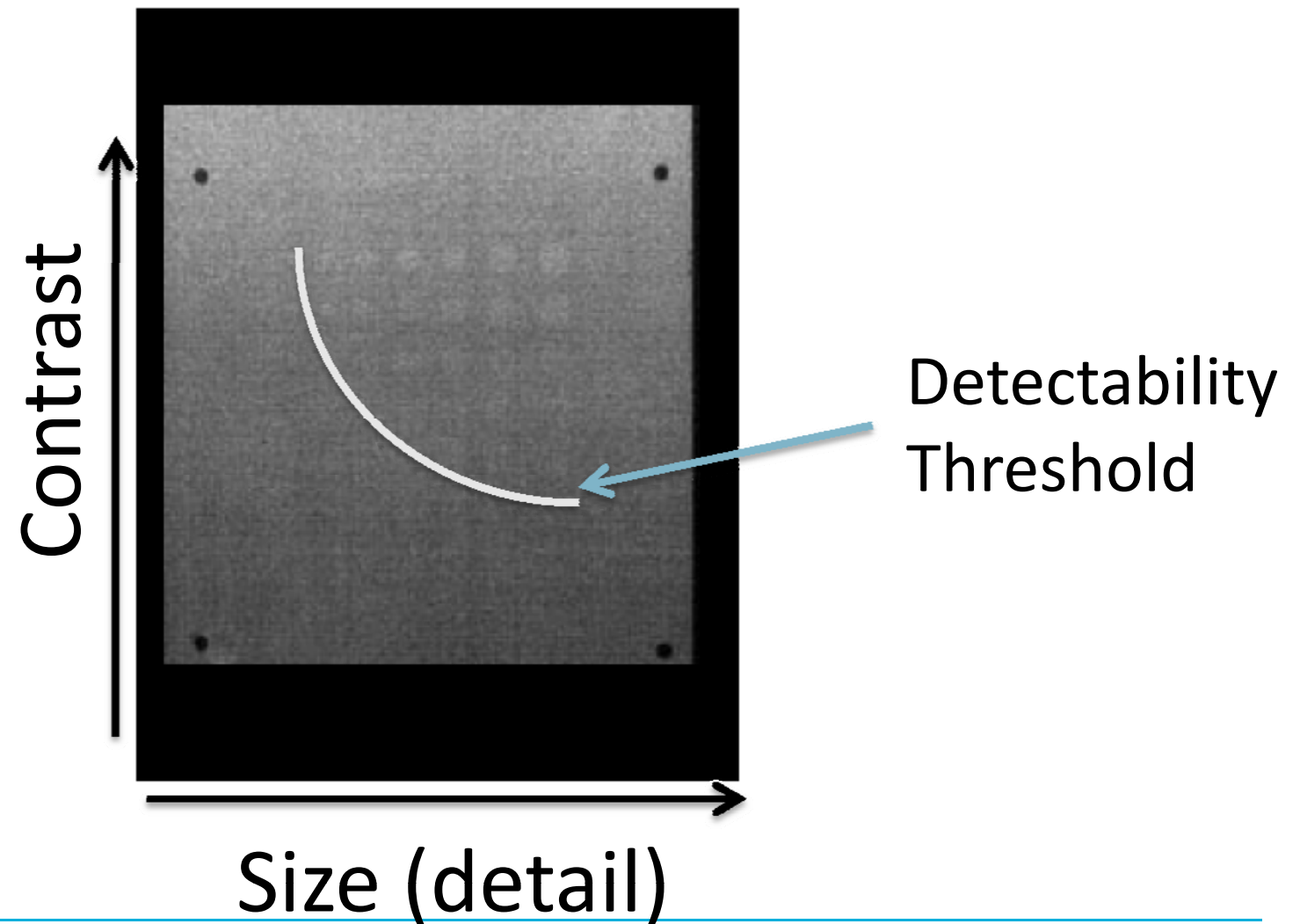
Point Spread Functions



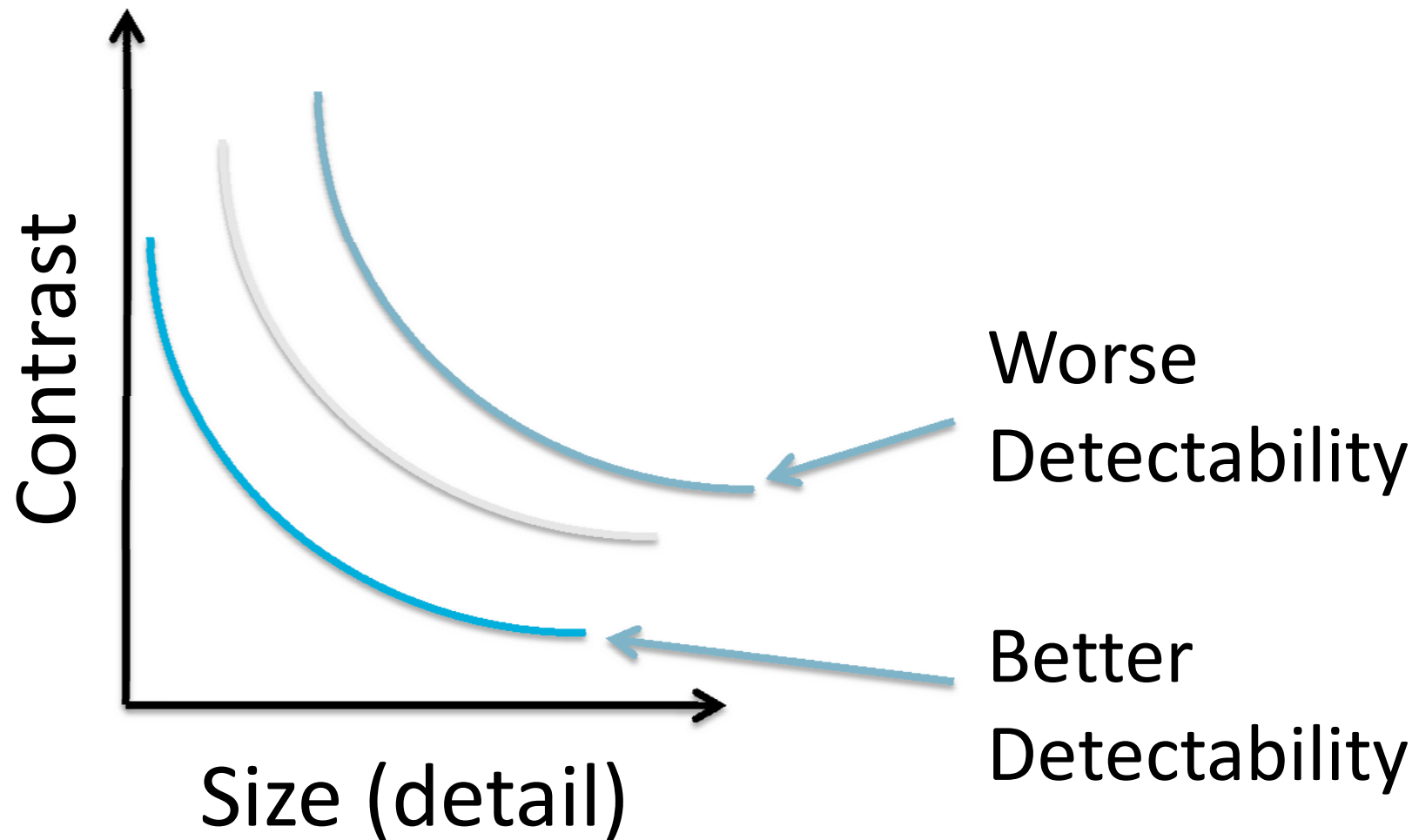
Contrast-Detail Phantom



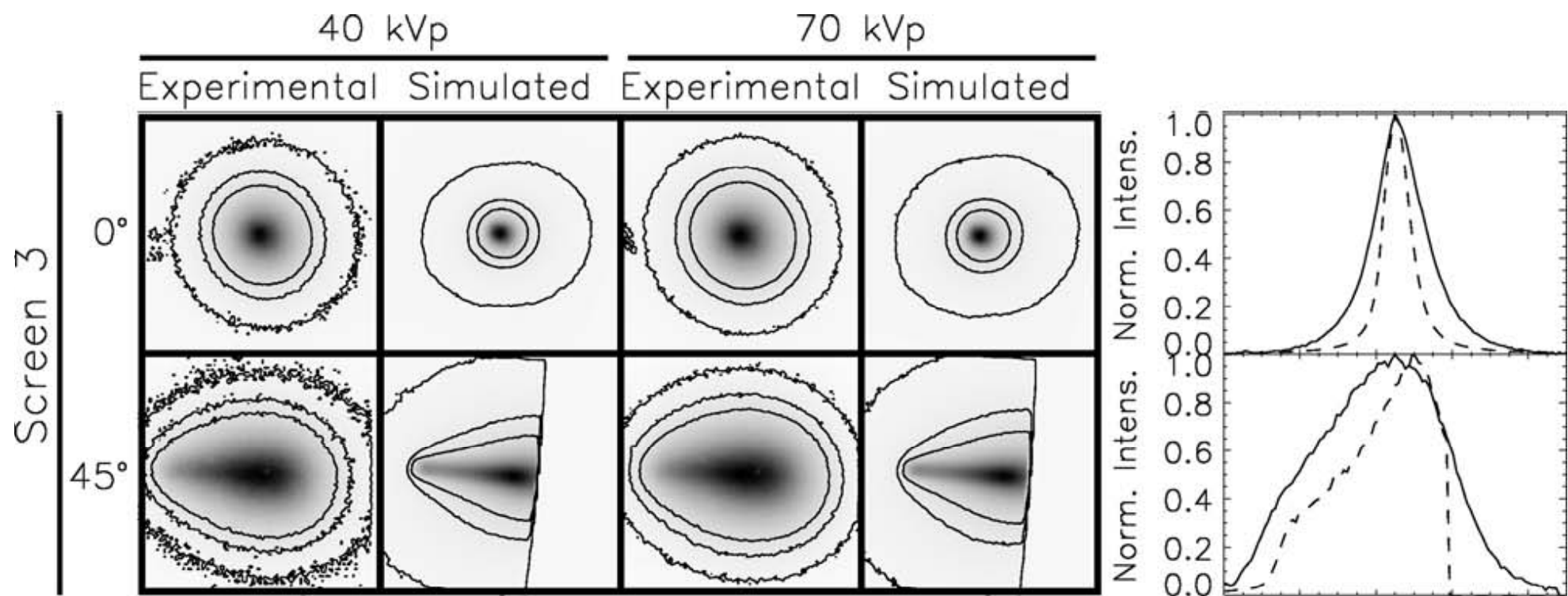
Contrast-Detail Phantom



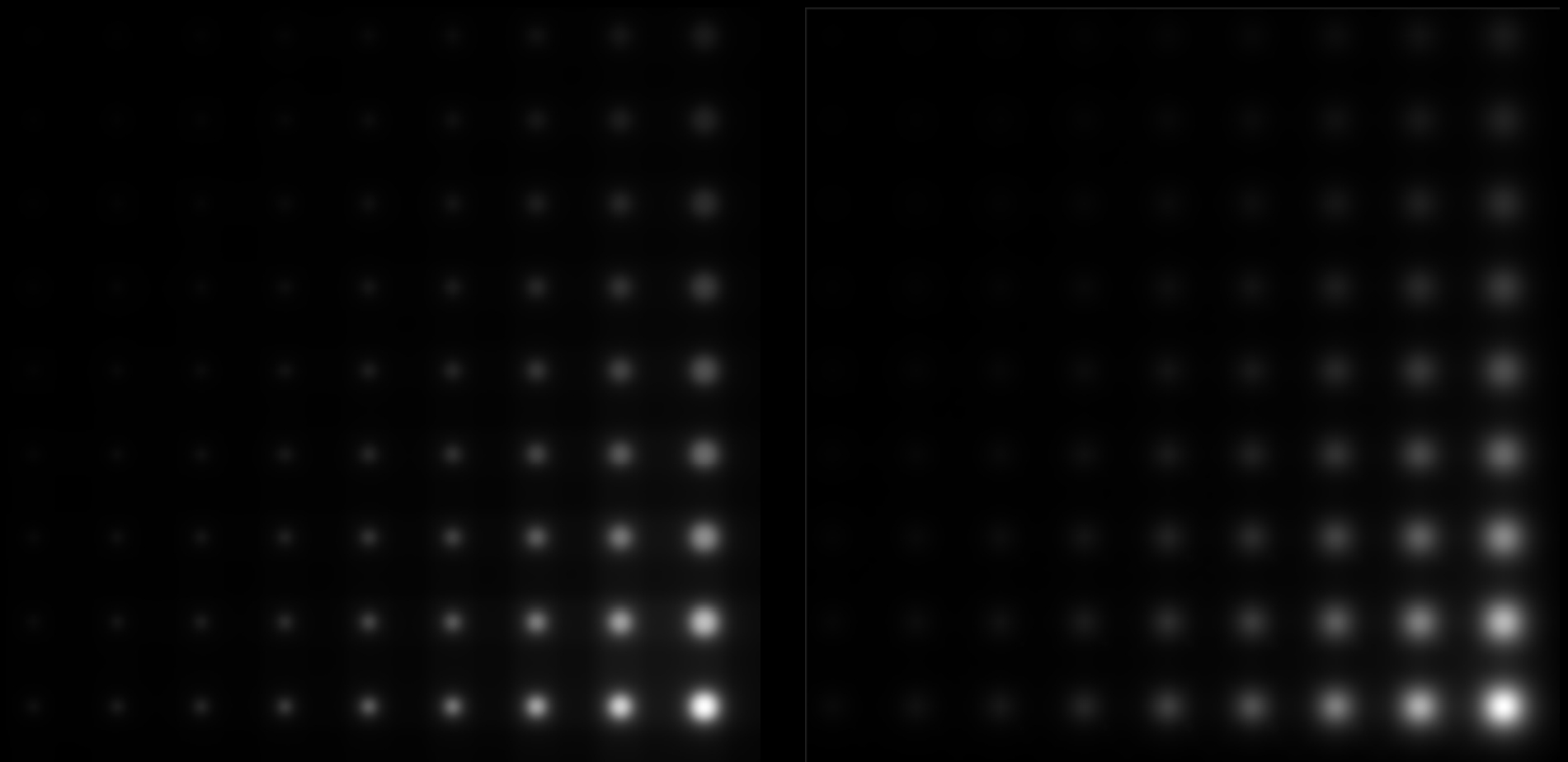
Contrast-Detail Curve



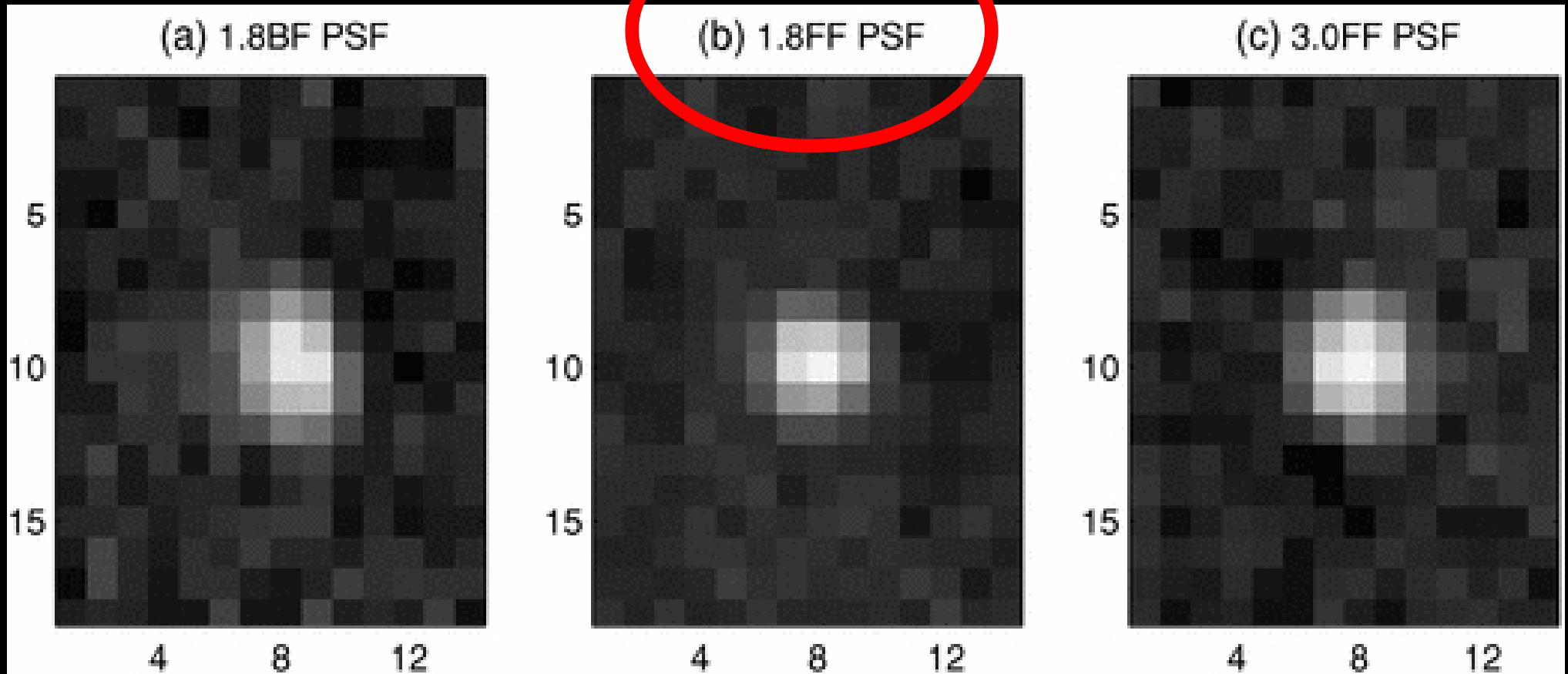
Point Spread Functions

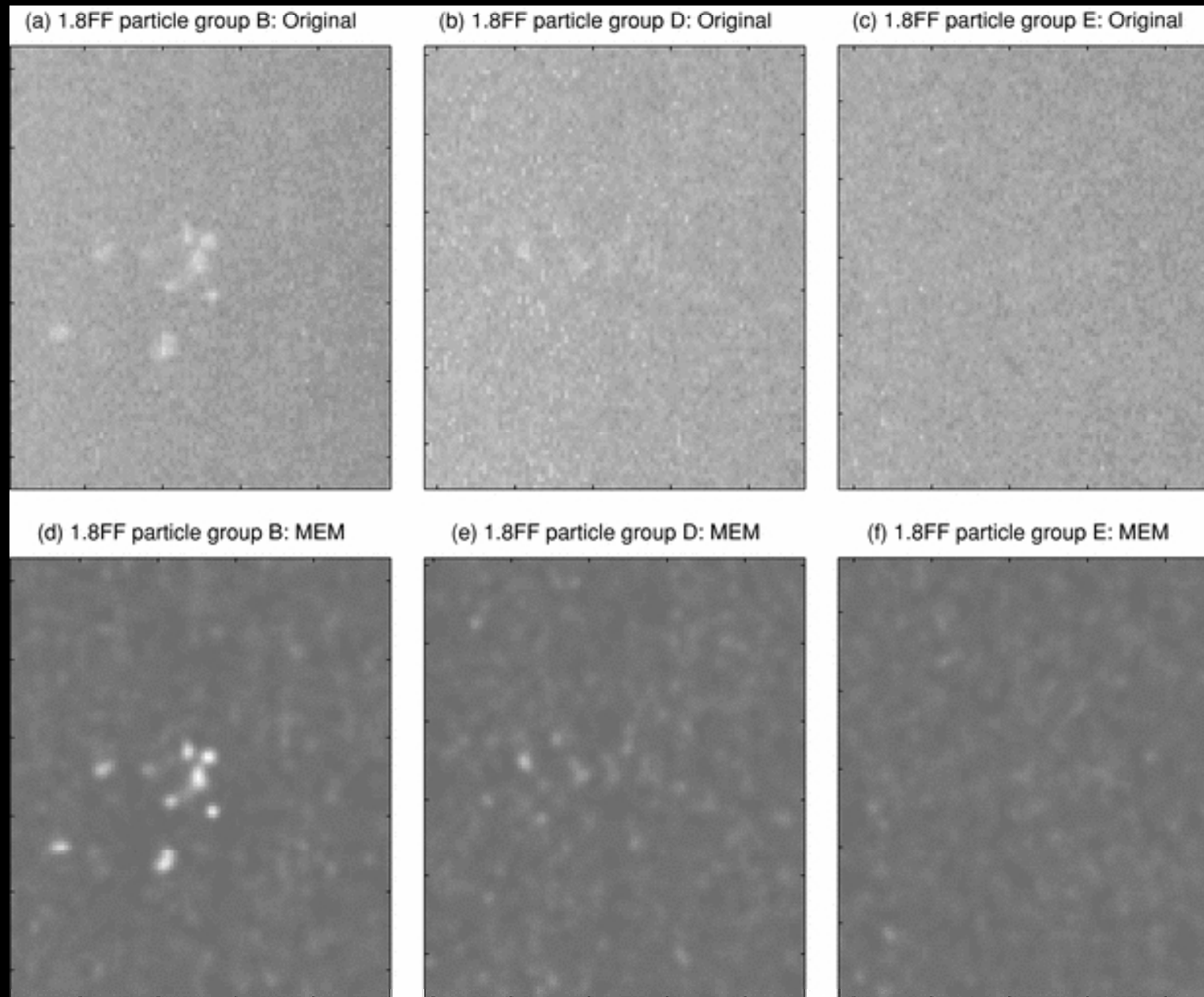


Contrast-Detail Phantom

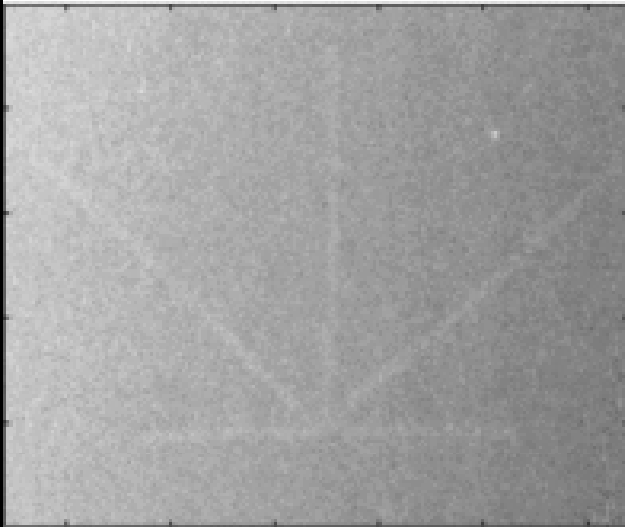


Example deblurring study

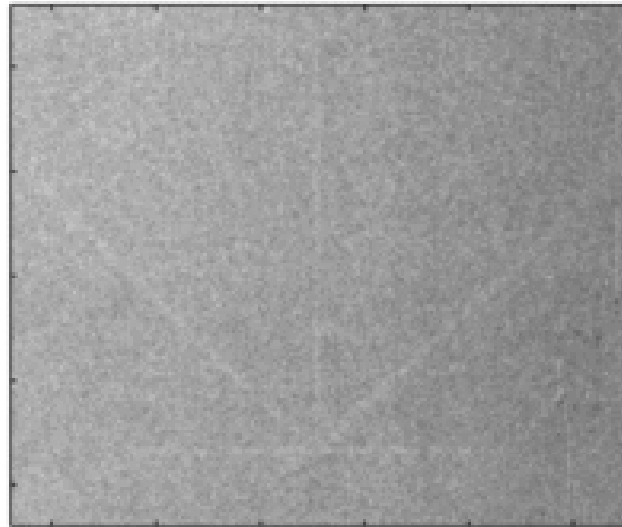




(a) 1.8FF filament group B: Original



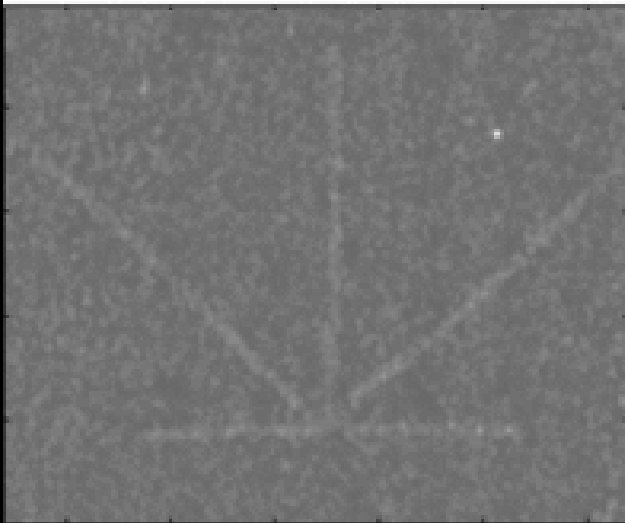
(b) 1.8FF filament group D: Original



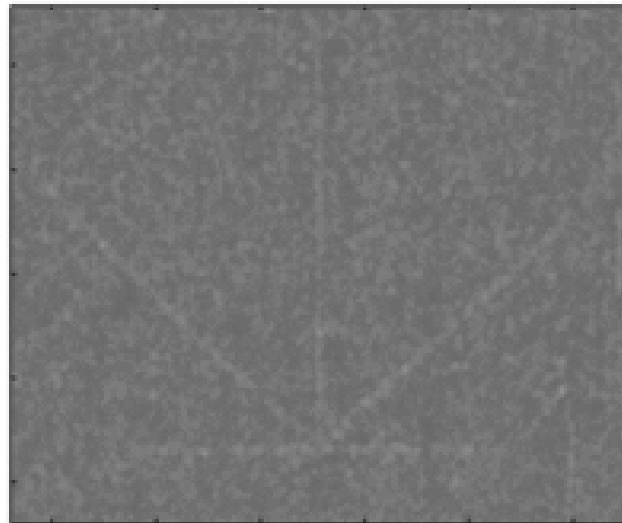
(c) 1.8FF filament group F: Original



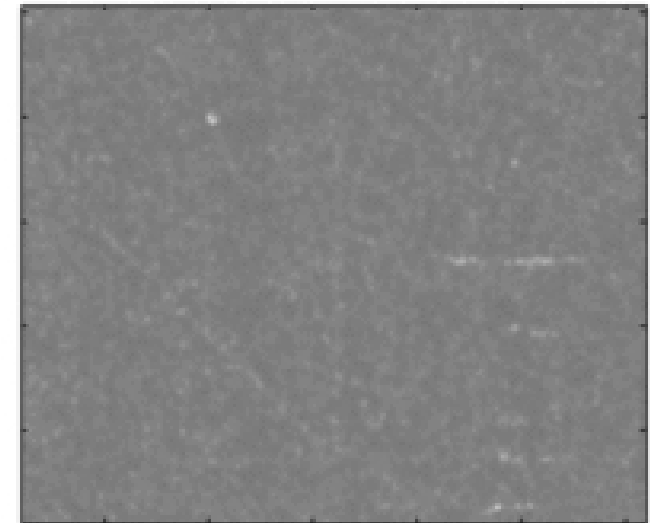
(d) 1.8FF filament group B: MEM

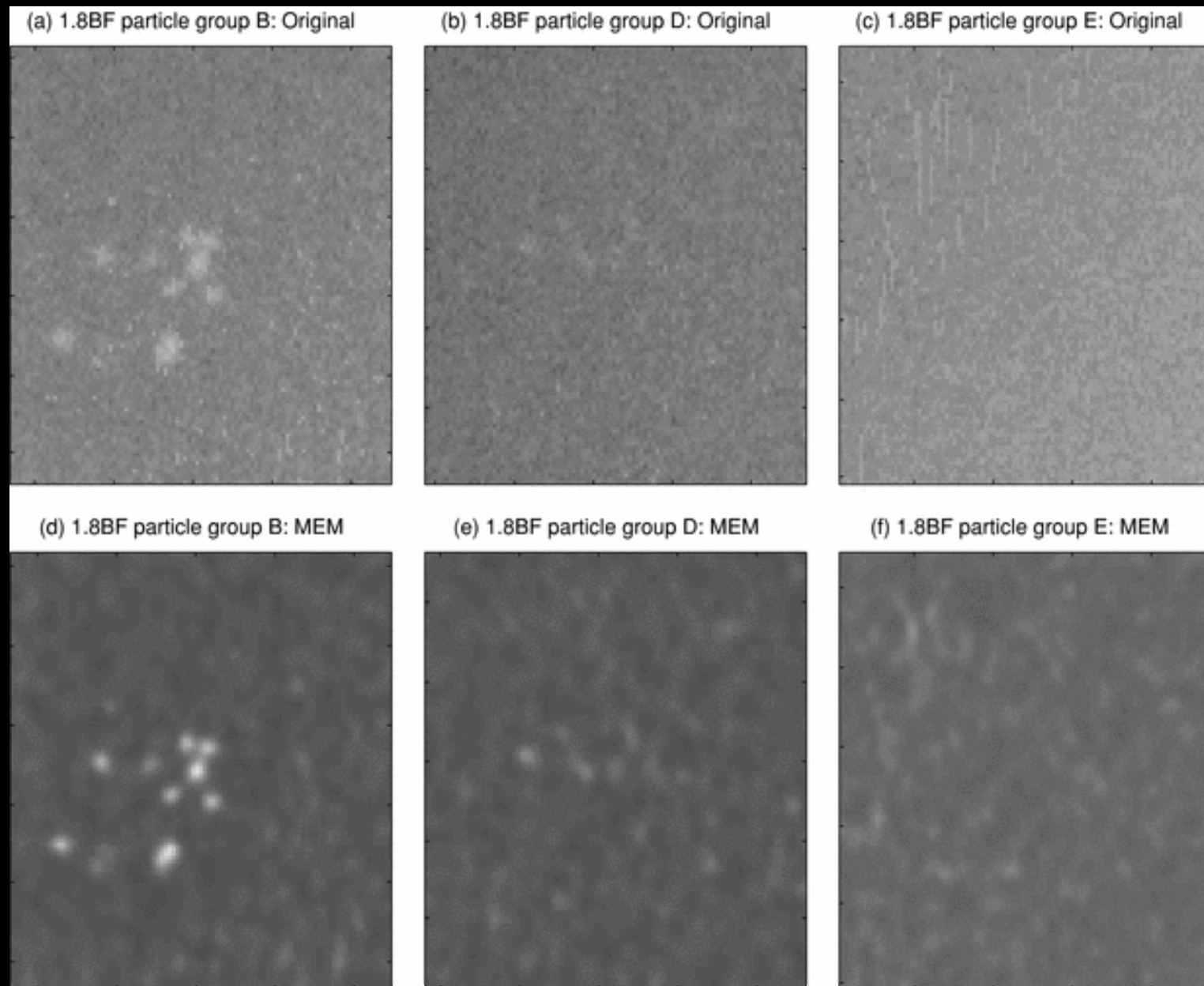


(e) 1.8FF filament group D: MEM



(f) 1.8FF filament group F: MEM





Observer scores

Mode	Original	MEM
1.8BF	51	77
1.8FF	54.5	81
3.0FF	79	104

Best metric

Receiver operating characteristics

But...

Expensive

Contrast-detail analysis

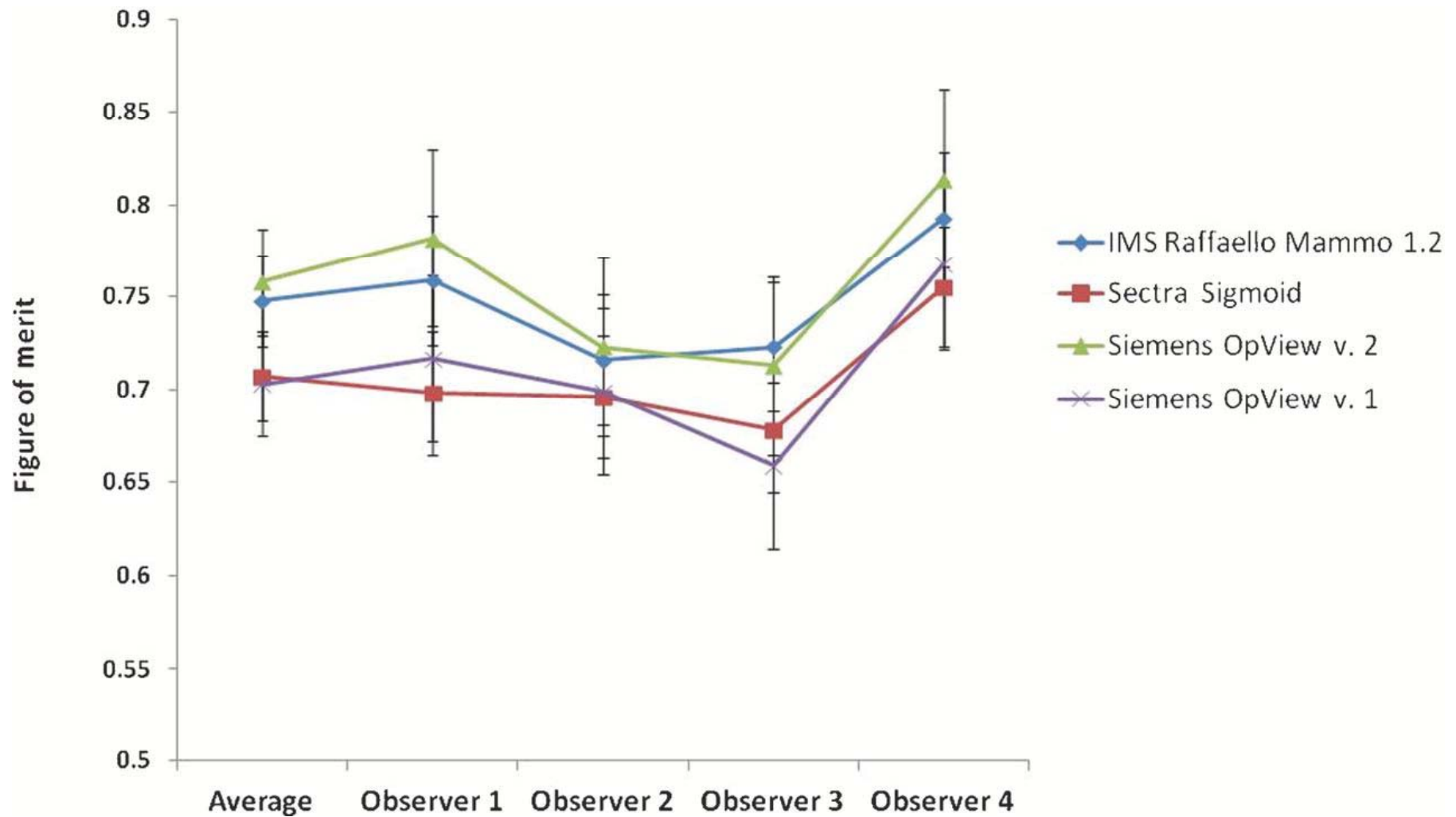
Pattern effect

Detection task (to be continued)

Visual Grading Analysis

2. Image criteria related to detector performance, exposure parameters and patient movement
 - 2.1 Clear reproduction of glandular tissue
 - 2.2 Clear reproduction of fibrous strands in fat tissue
 - 2.3 Clear reproduction of vascular structures in fat tissue
 - 2.4 Clear reproduction of pectoral muscle margin
 - 2.5 Clear reproduction of calcifications, when present
 - 2.6 Acceptable noise level in the reproduction of the pectoral muscle
3. Overview judgement related to either screening or diagnostic procedures
 - 3.1 Is image quality sufficient for early breast cancer detection?

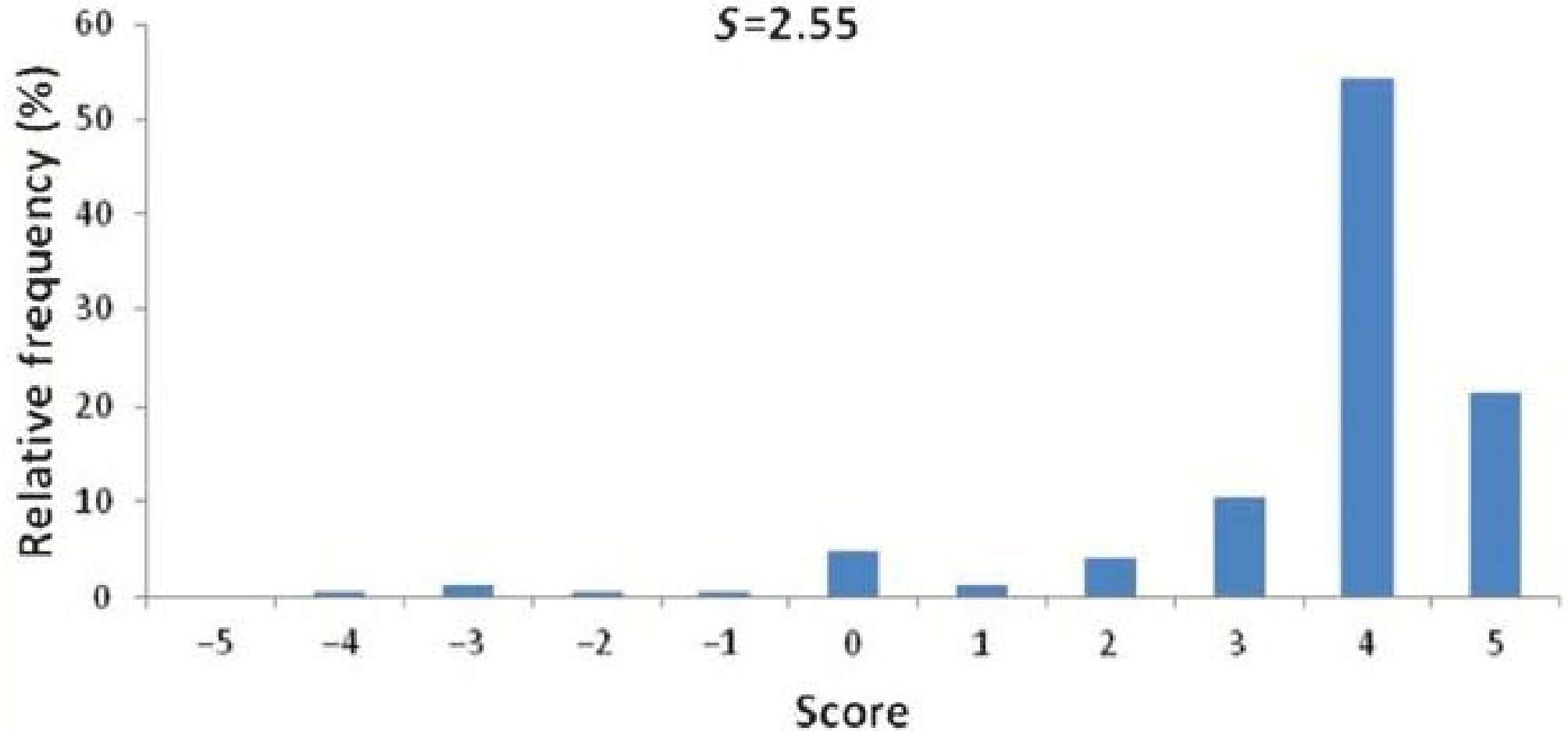
JAFROC Results



VGA Results

Siemens OpView v. 2 vs IMS Raffaello

$S=2.55$



UNCERTAINTY: Engineering

Imperfect detector response

UNCERTAINTY: Engineering

PSF modeled
experimentally and
simulation

UNCERTAINTY: Engineering

True PSF(s) unknown

UNCERTAINTY: Engineering

Single PSF is an
approximation

UNCERTAINTY: Engineering

Blind deconvolution (?)

UNCERTAINTY: Engineering

How should we
evaluate image
quality?

UNCERTAINTY: Engineering

What should we aim to improve?

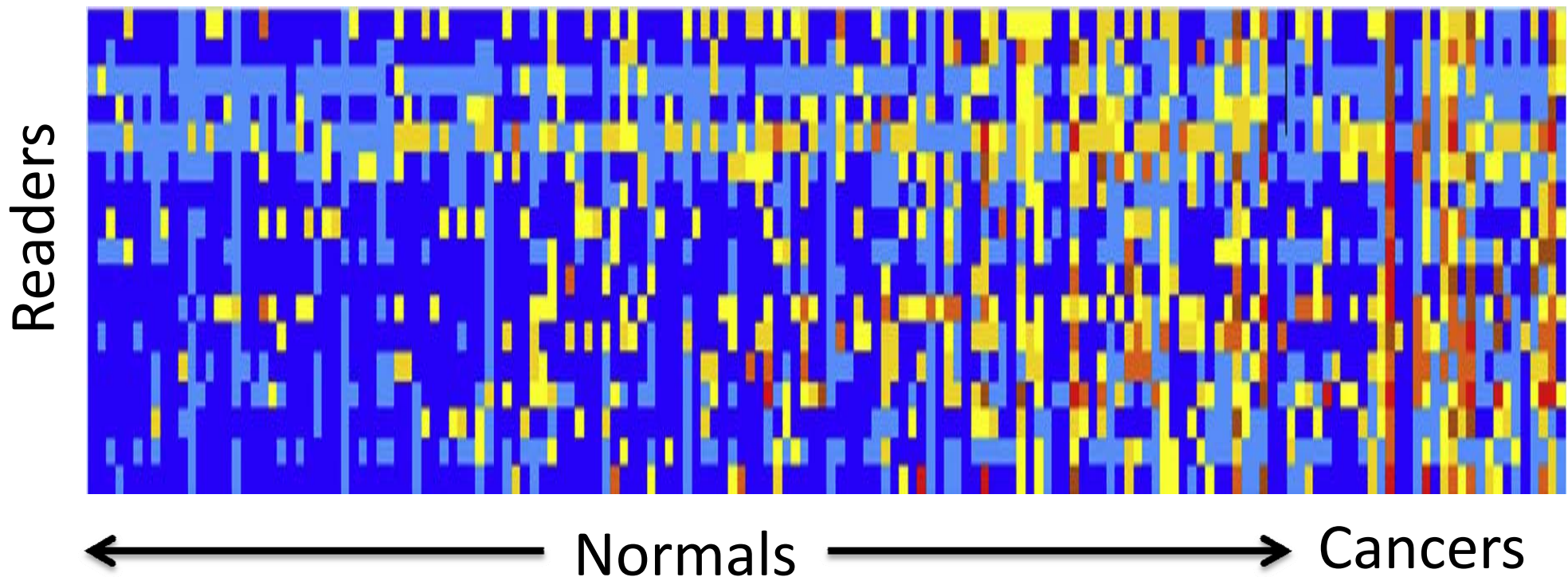
UNCERTAINTY: PERCEPTION



Radiologists are not perfect...

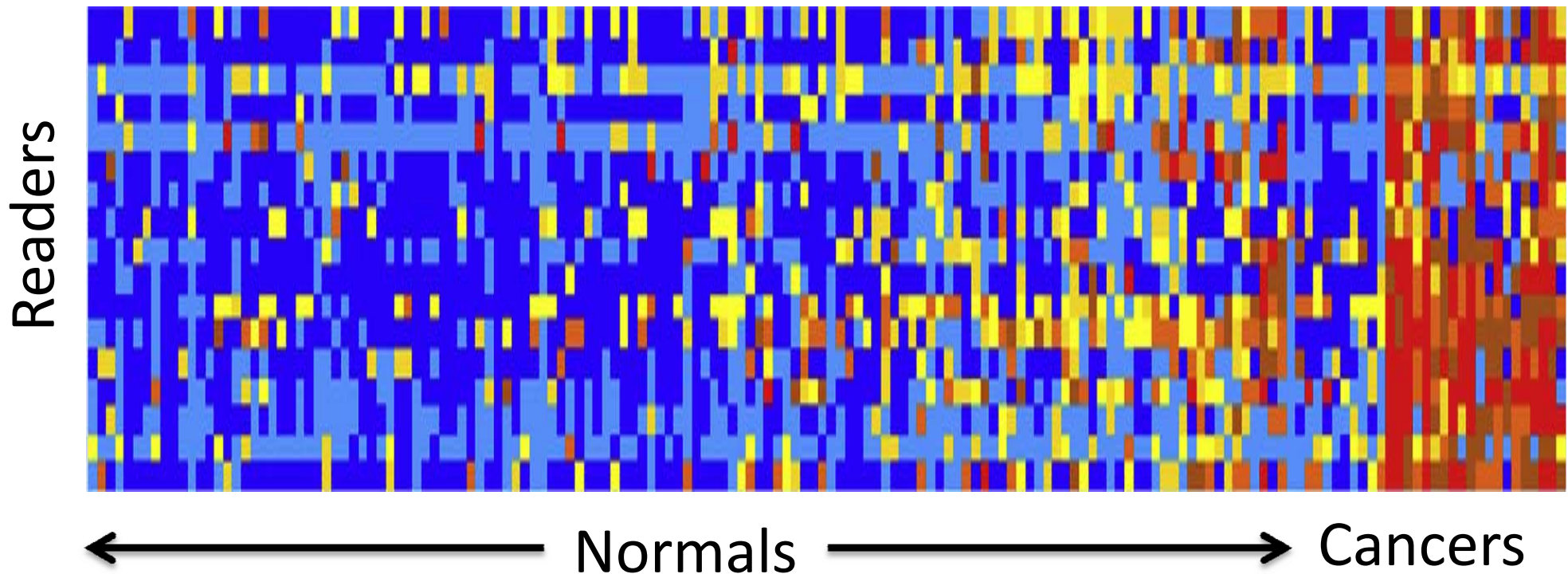
...and their imperfections vary

Inter-reader variability



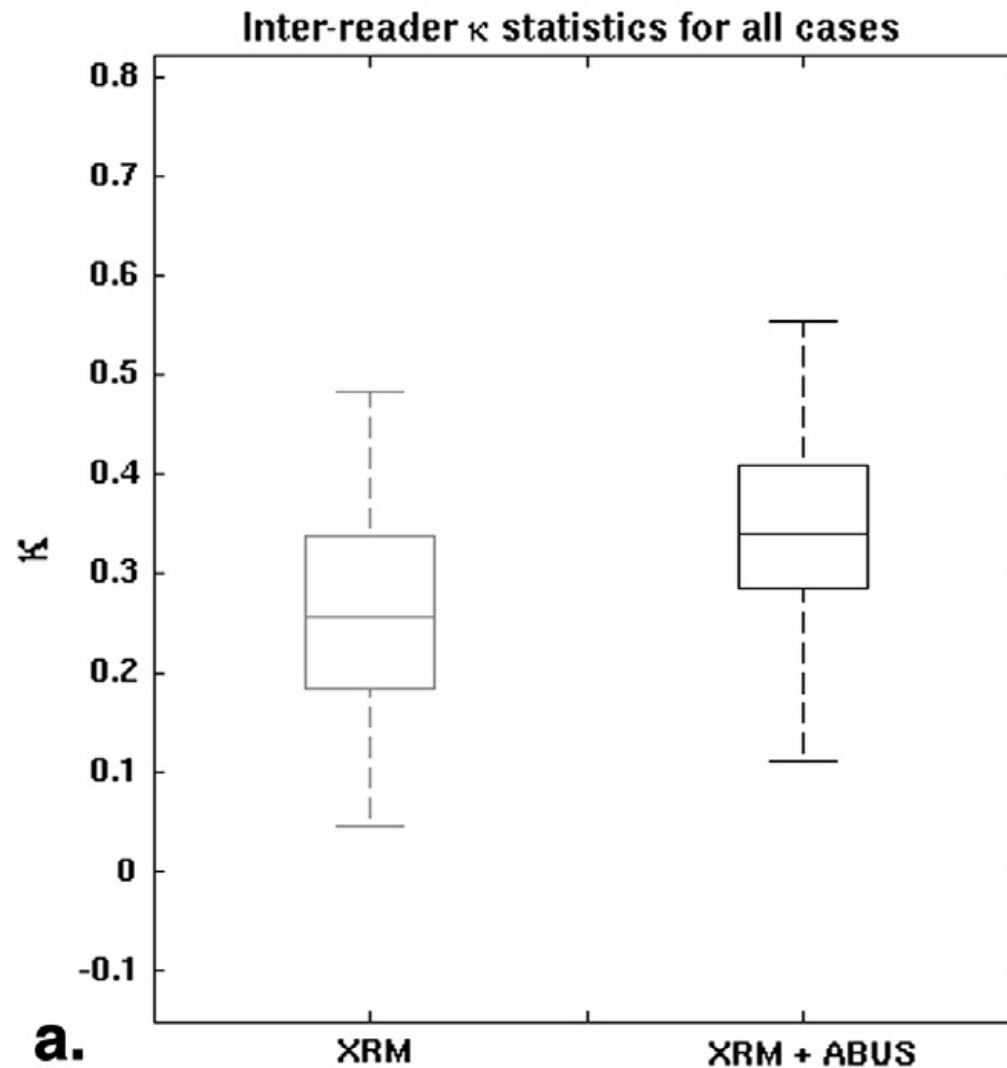
Mammography alone, 17 readers, 164 cases

Inter-reader variability



Mammo + ABUS, 17 readers, 164 cases

Inter-reader variability



Inter-reader variability

Mammography

8 readers, 45 cases

2 reads per reader per case

Inter-reader variability

Inter-reader kappa: 0.45 (first read)
 0.44 (second read)
 (moderate)

But also...

Intra-reader variability

Intra-reader kappa: 0.35 – 0.67
 mean: 0.56
 (moderate)

What does it take to detect a lesion?

One of the radiologists later admitted, “I just didn’t see it.”

Three steps to detection

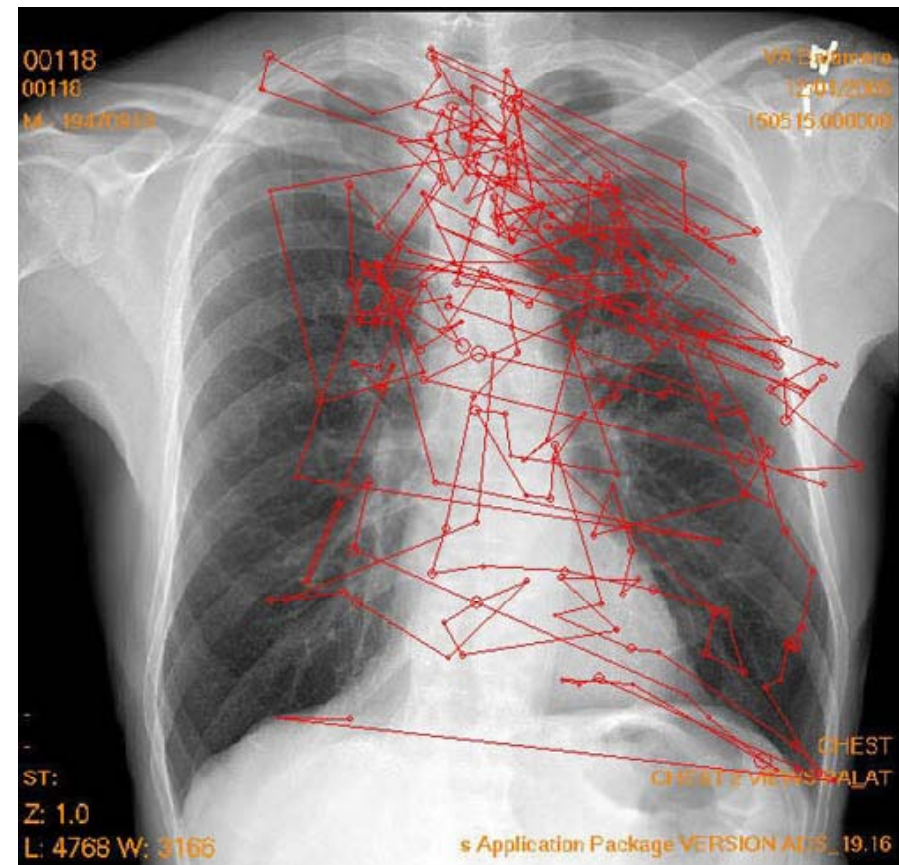
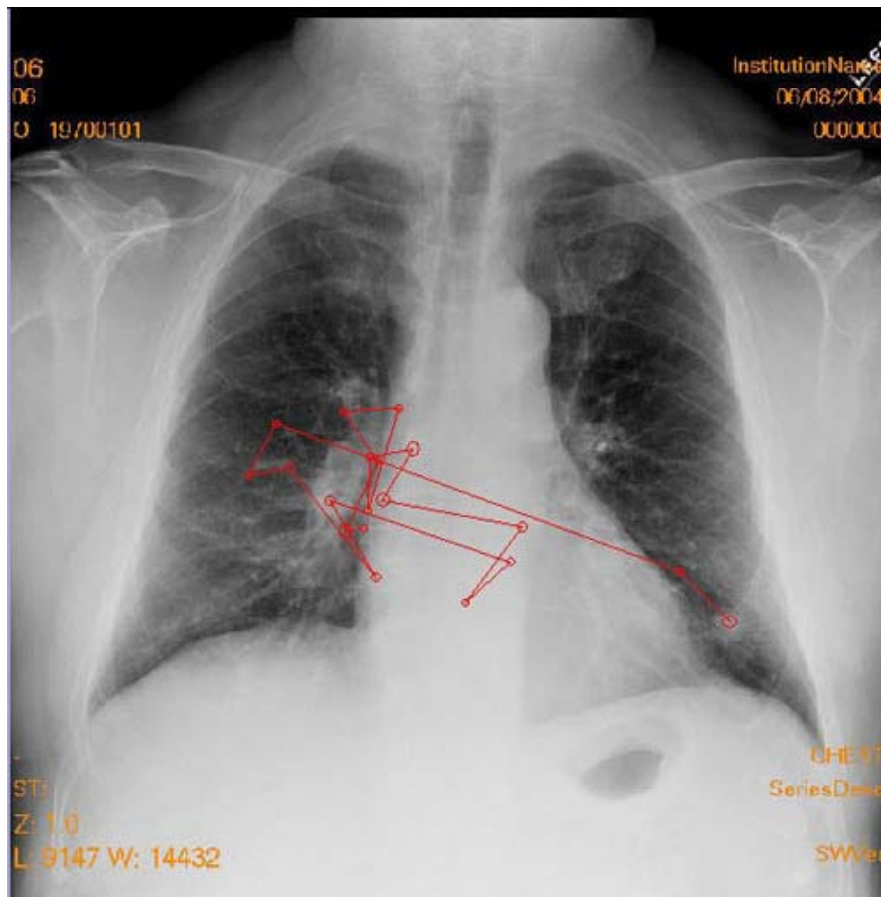
Search

Recognition

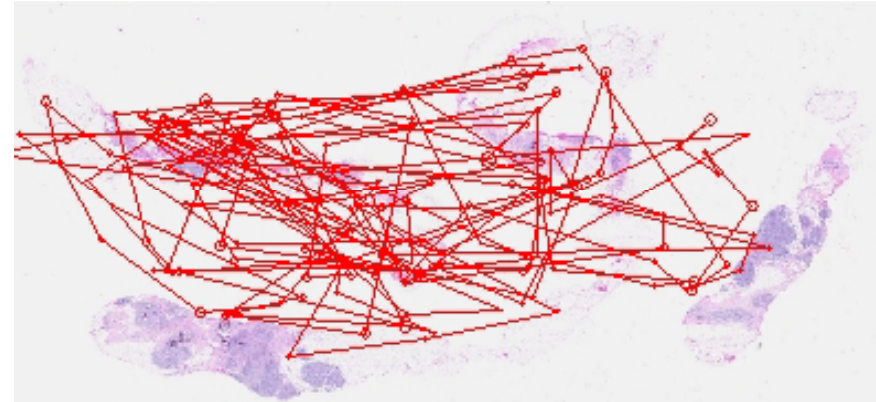
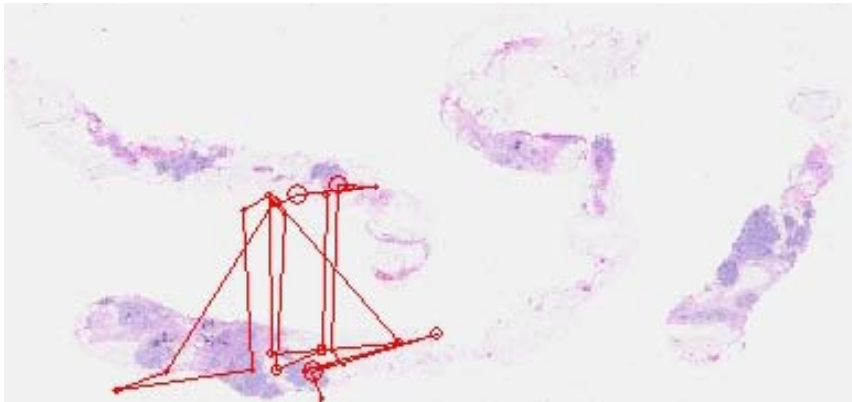
Decision

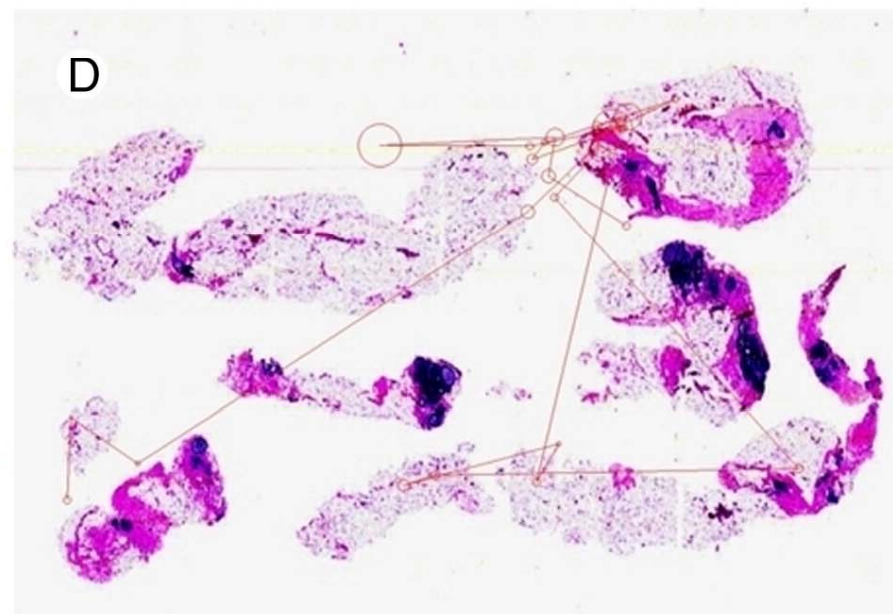
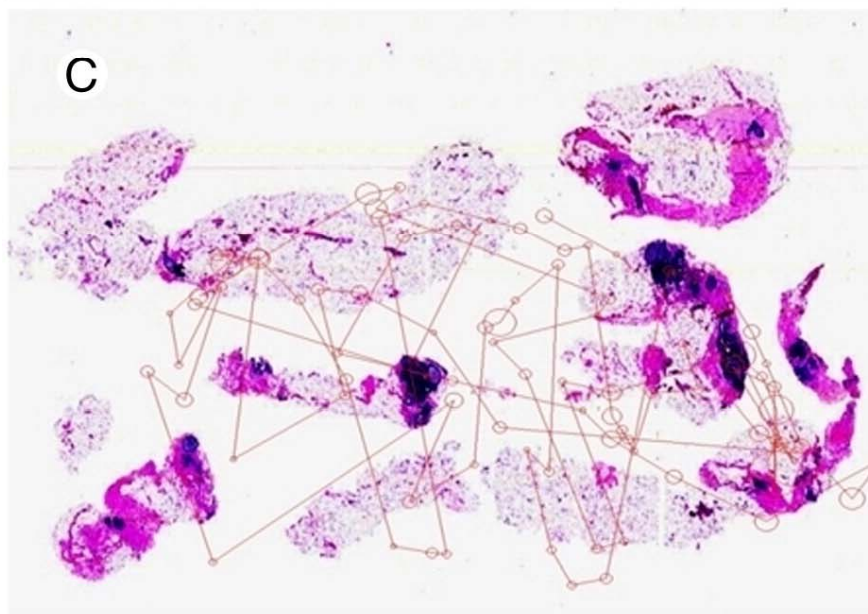
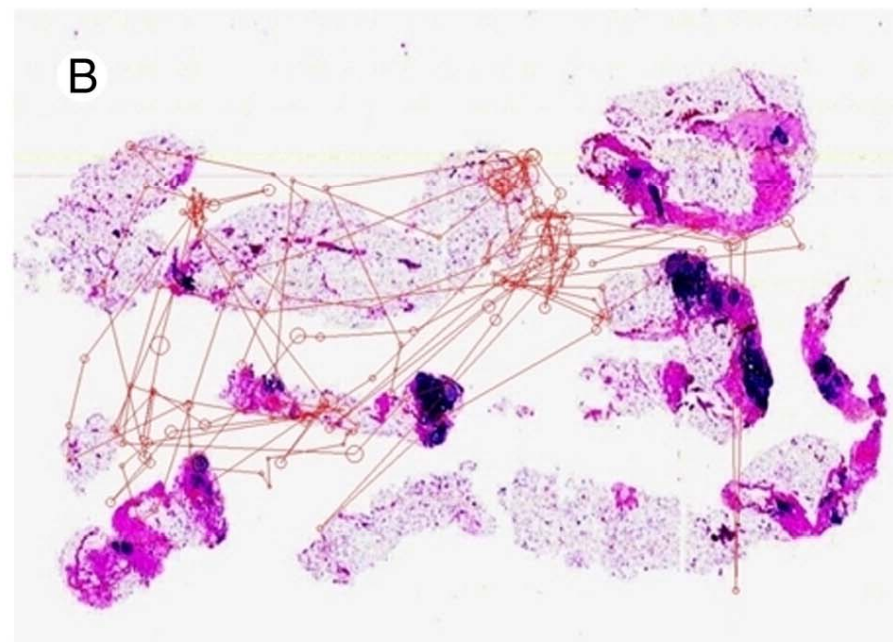
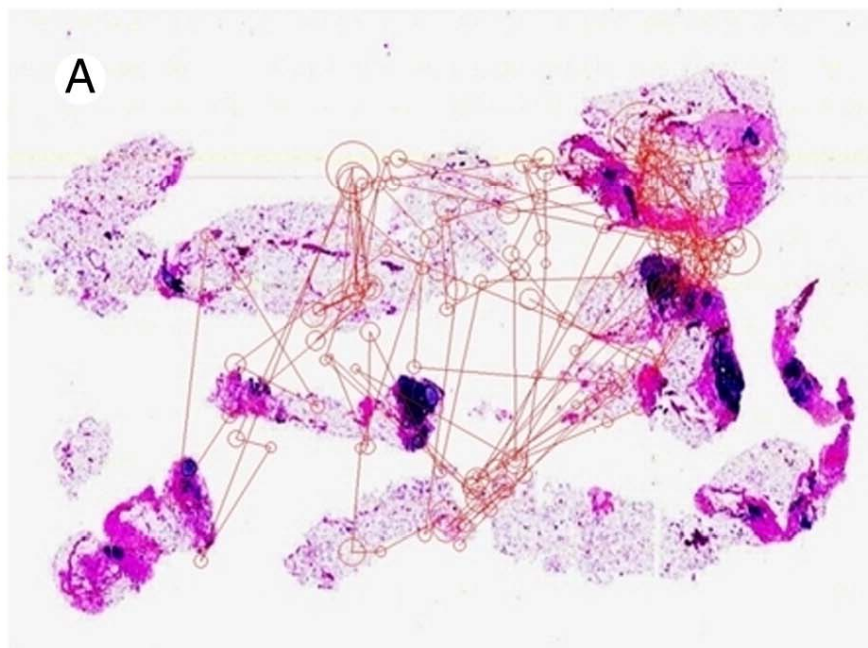
Search: Did the eyes pass by the lesion?

Search



Search





Recognition: Was the lesion recognized as such?

Wasting time looking at irrelevant areas...

	Year 1	Year 2	Year 3	Year 4
Relevant	96.25%	99.58%	99.17%	100%
Not relevant	3.75%	0.42%	0.83%	0%

Decision: Is what I'm looking at a cancer?

Reasons for false negatives

	Experienced	Inexperienced
False negatives	8	21
Search	24%	29%
Recognition	24%	42%
Decision	52%	29%

False negatives: mammo vs tomo

	Tomo + Mammo -	Tomo - Mammo +
Visibility	13	0
Radiographic appearance	3	1
Interpretative error	3	6

**Don't make lesions just
more apparent so they
can be seen....**

**...make them clearer so
they can be characterized...**

UNCERTAINTY: Perception

(for now?) Humans
read radiology images

UNCERTAINTY: Perception

Mistakes happen
(differently!)

UNCERTAINTY: Perception

Our research should
pay attention to these
perception results

UNCERTAINTY: EPIDEMIOLOGY

Screening for breast cancer works...

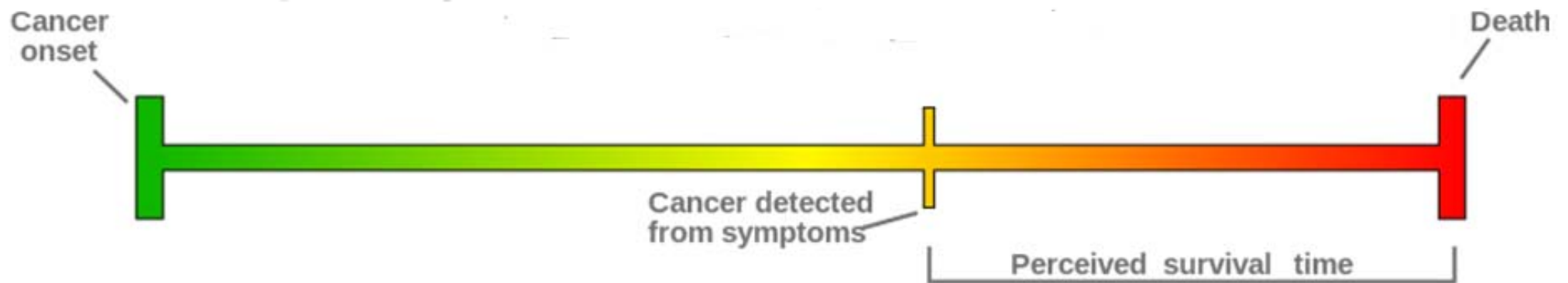
....right?

Sure!

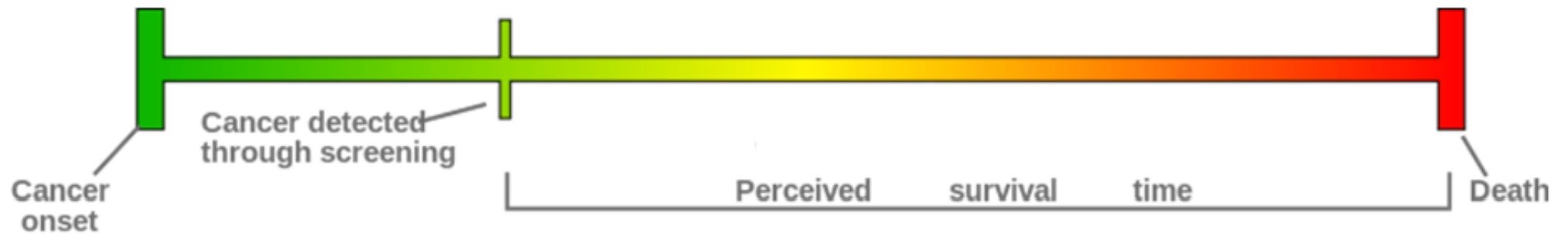
People live longer!

"The five-year survival rate for all cancers improved from 51 percent in the early 1980s to almost 60 percent in the early 1990s. . . . since the 1971 National Cancer Act, much of the research into early cancer detection and treatment has paid off."

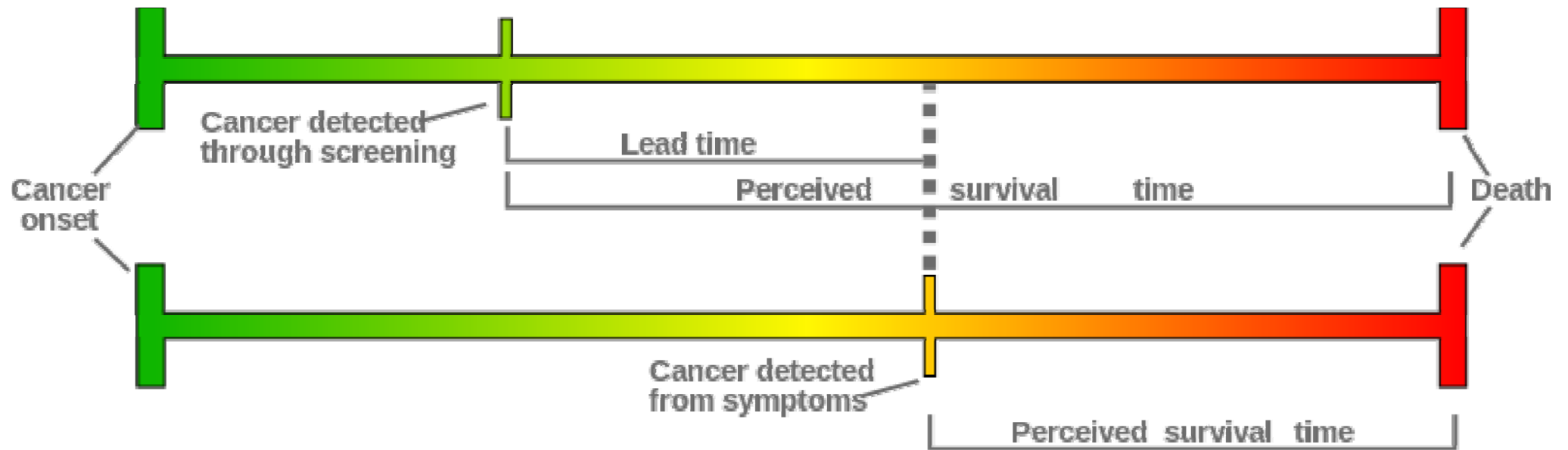
Take one cancer patient...



Take another cancer patient...

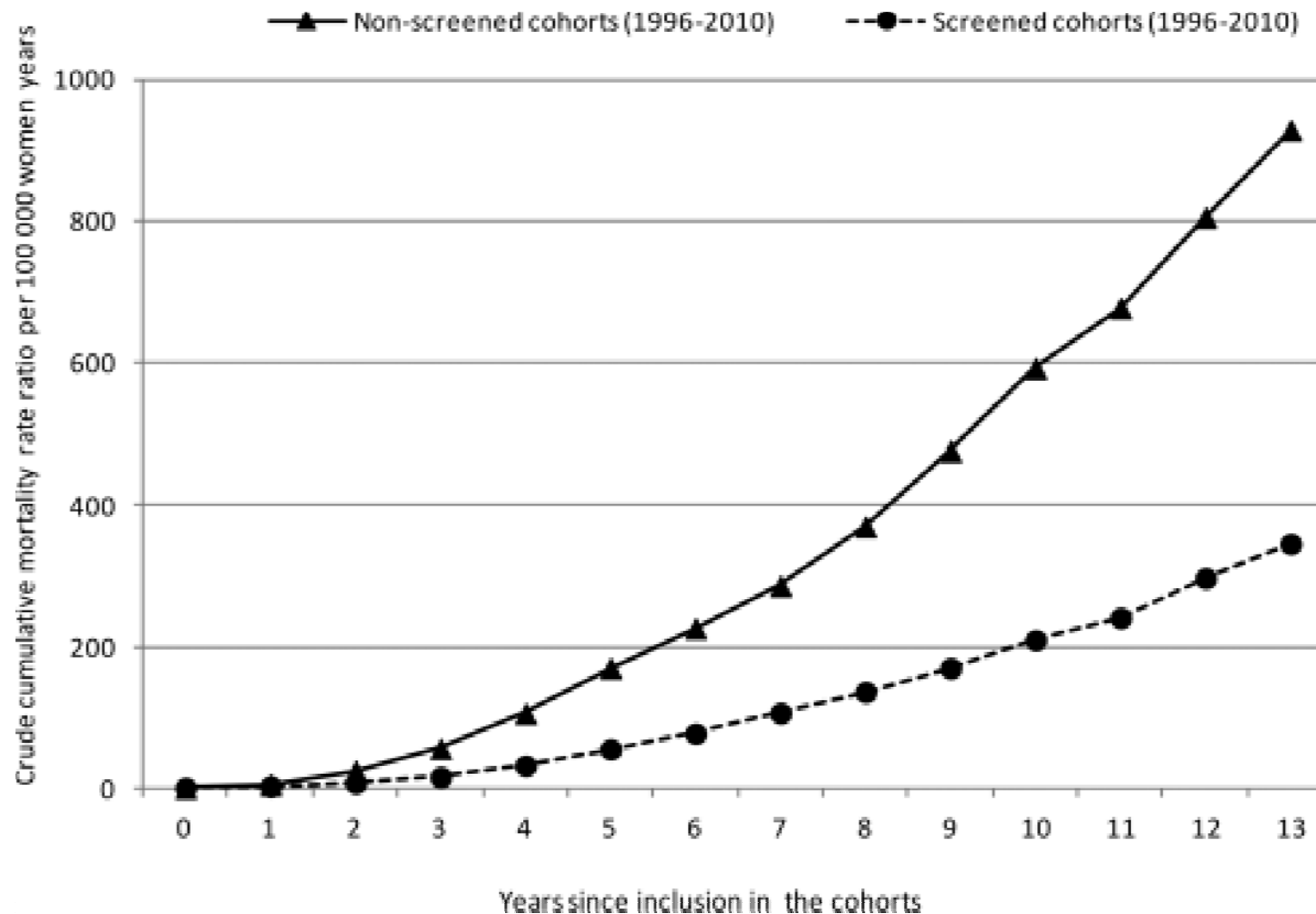


Lead time bias



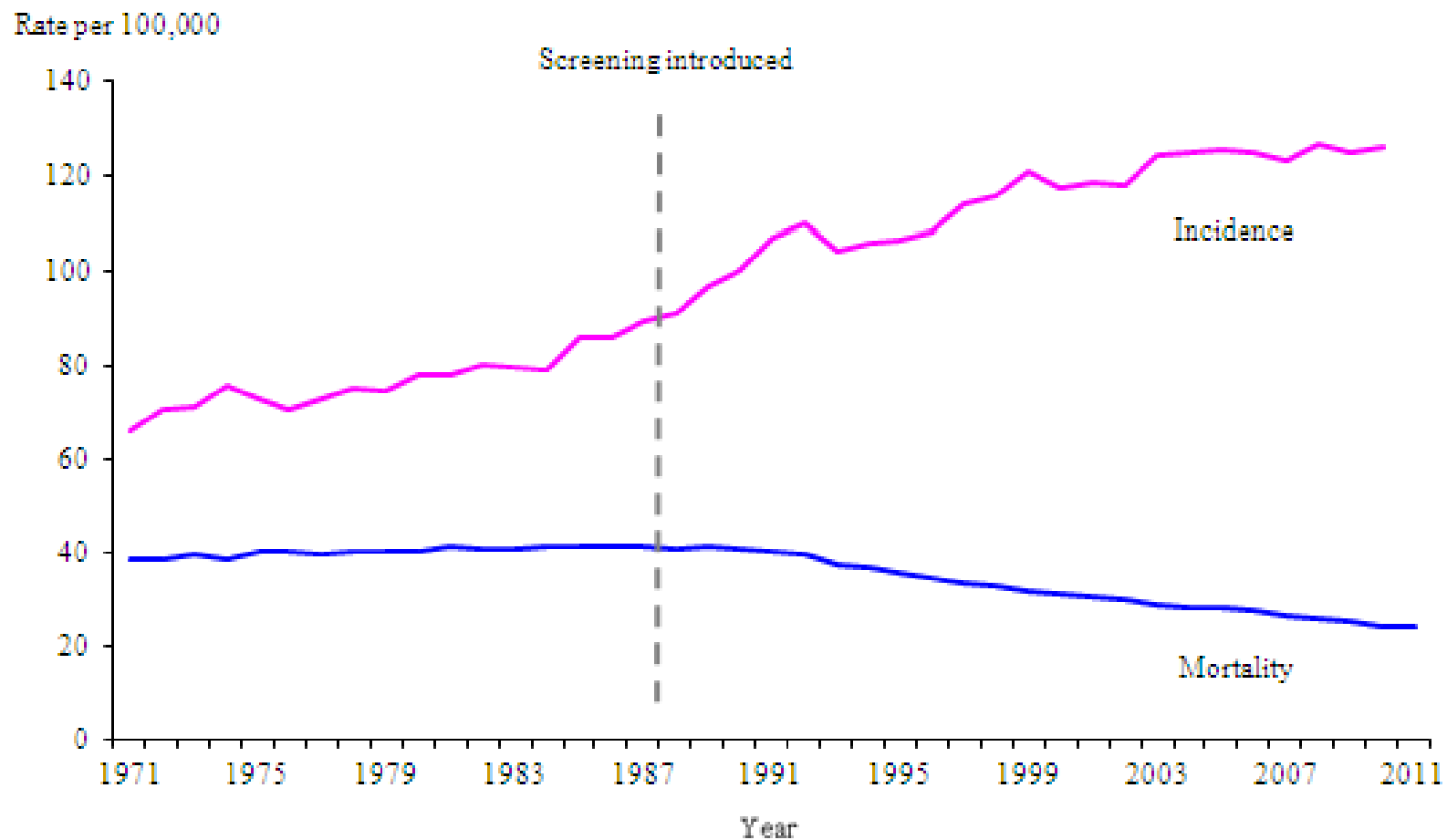
X-year survival can't be
used for determining
screening
effectiveness

In some cases two cohorts are available



Comparison pre-screening

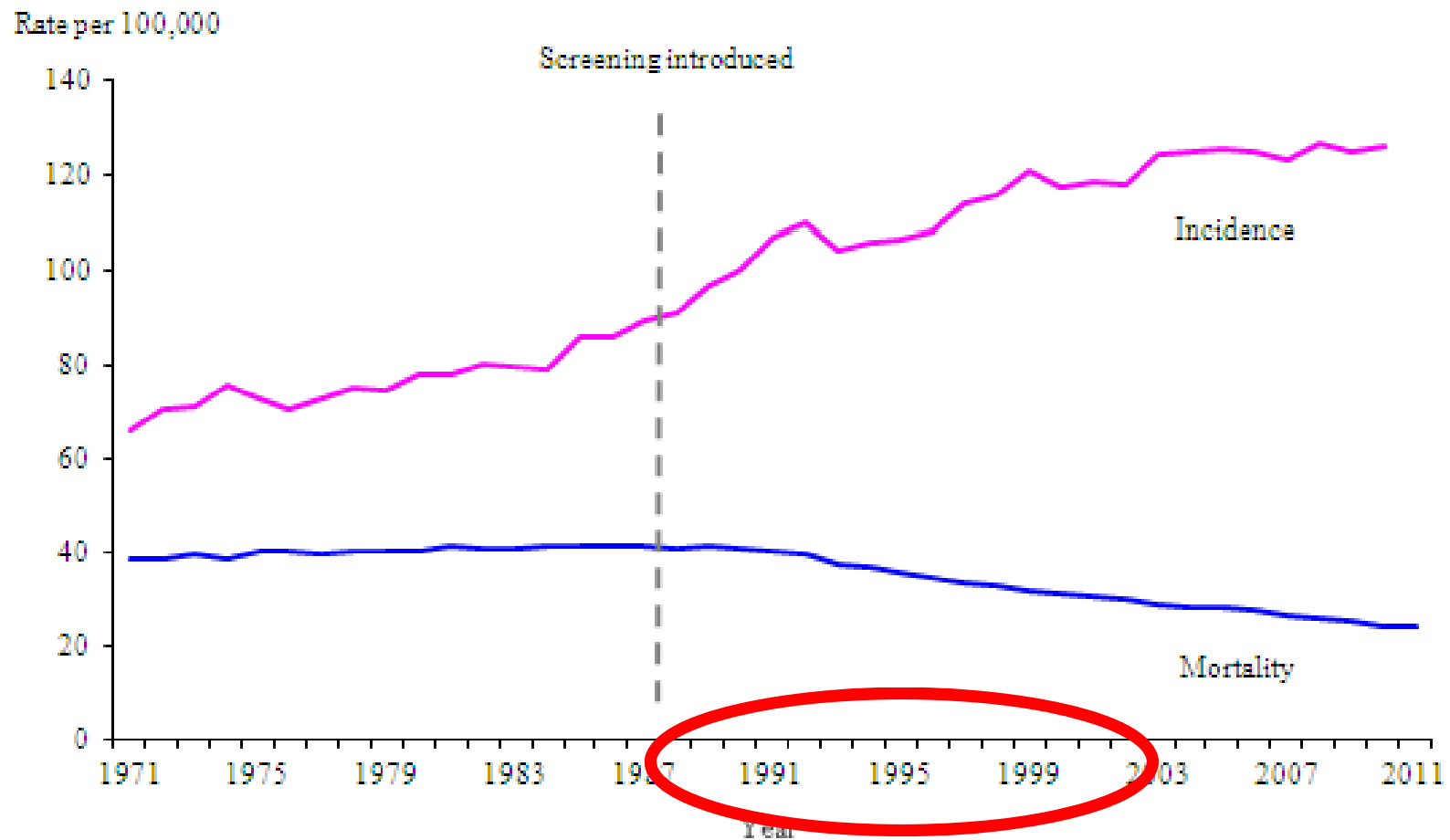
Female breast cancer in England: incidence and mortality



Source: Office for National Statistics

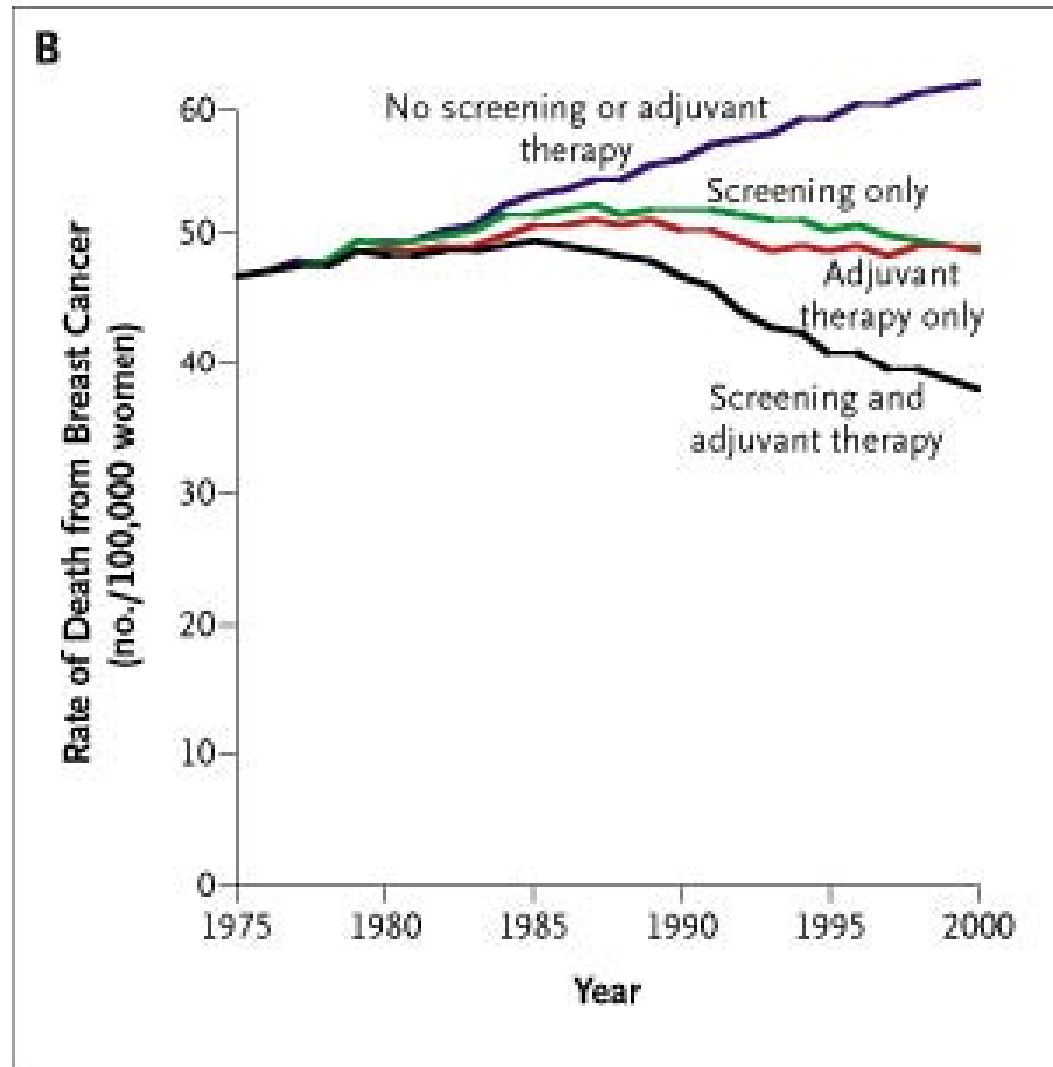
but...

Female breast cancer in England: incidence and mortality



Source: Office for National Statistics

also...



Screening or therapy?



Important and challenging

Incidence must be the
same
(or corrected for)

Example:

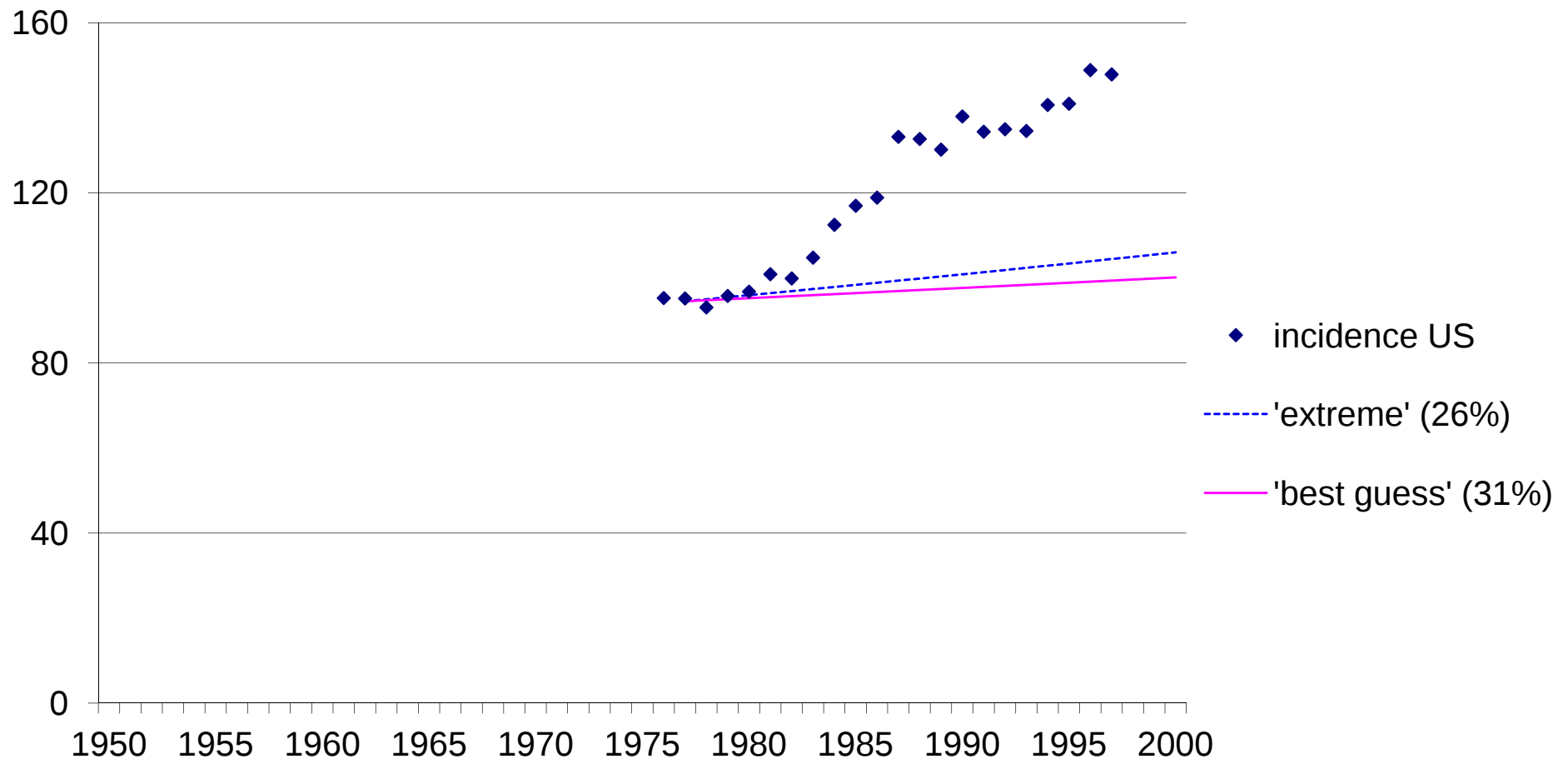
Modeling incidence to
estimate
over-diagnosis

*“in 2008, breast cancer was
overdiagnosed in more than 70,000
women...31% of all breast cancers
diagnosed.”*

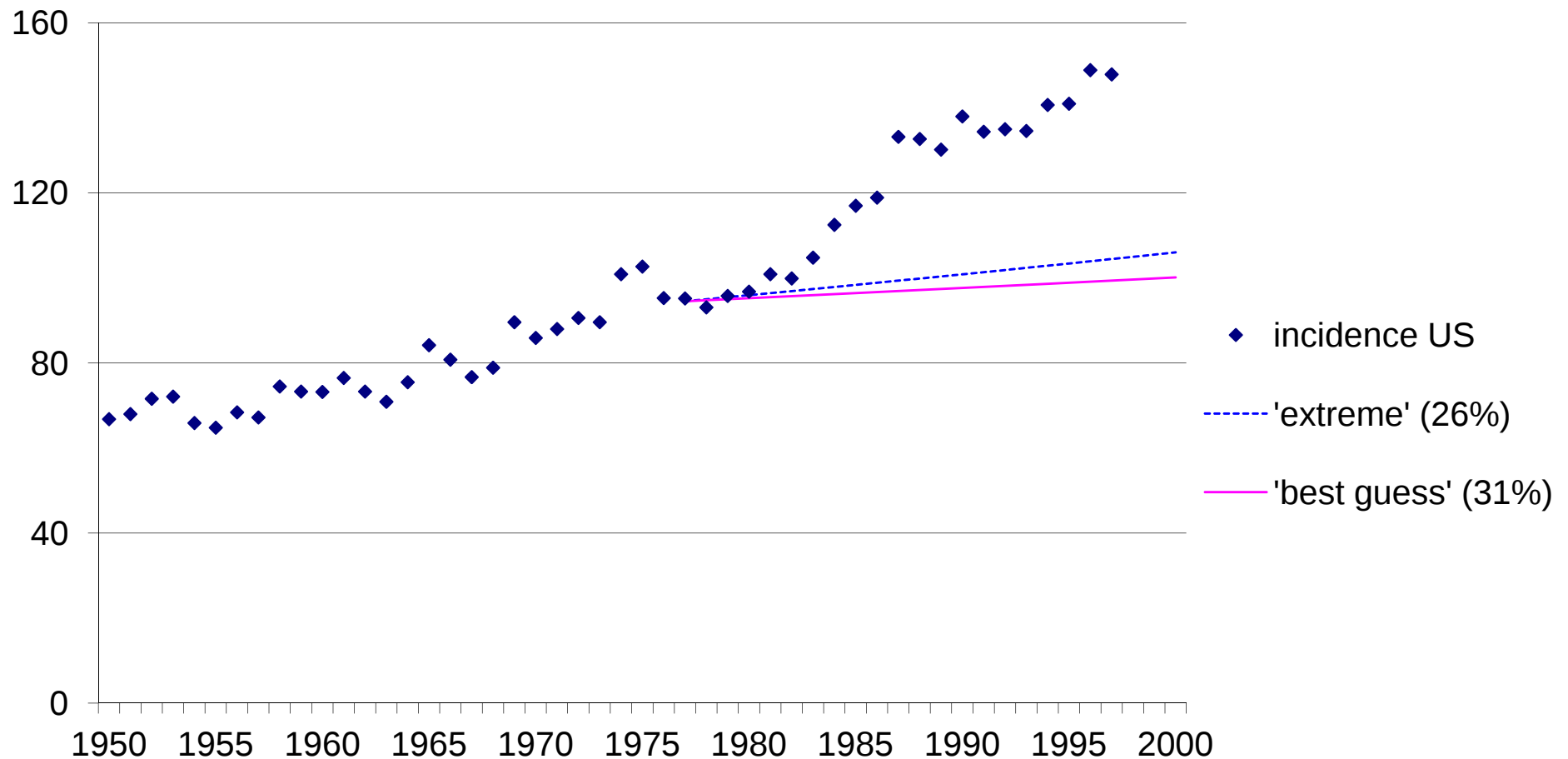
Underlying breast cancer risk

Estimate	Incidence increase (%/yr)	Overdiagnosis
Base case	constant	
Best guess	0.25%	31%
Extreme assumption	0.50%	26%
Very extreme assumption	0.5% + highest baseline	22%

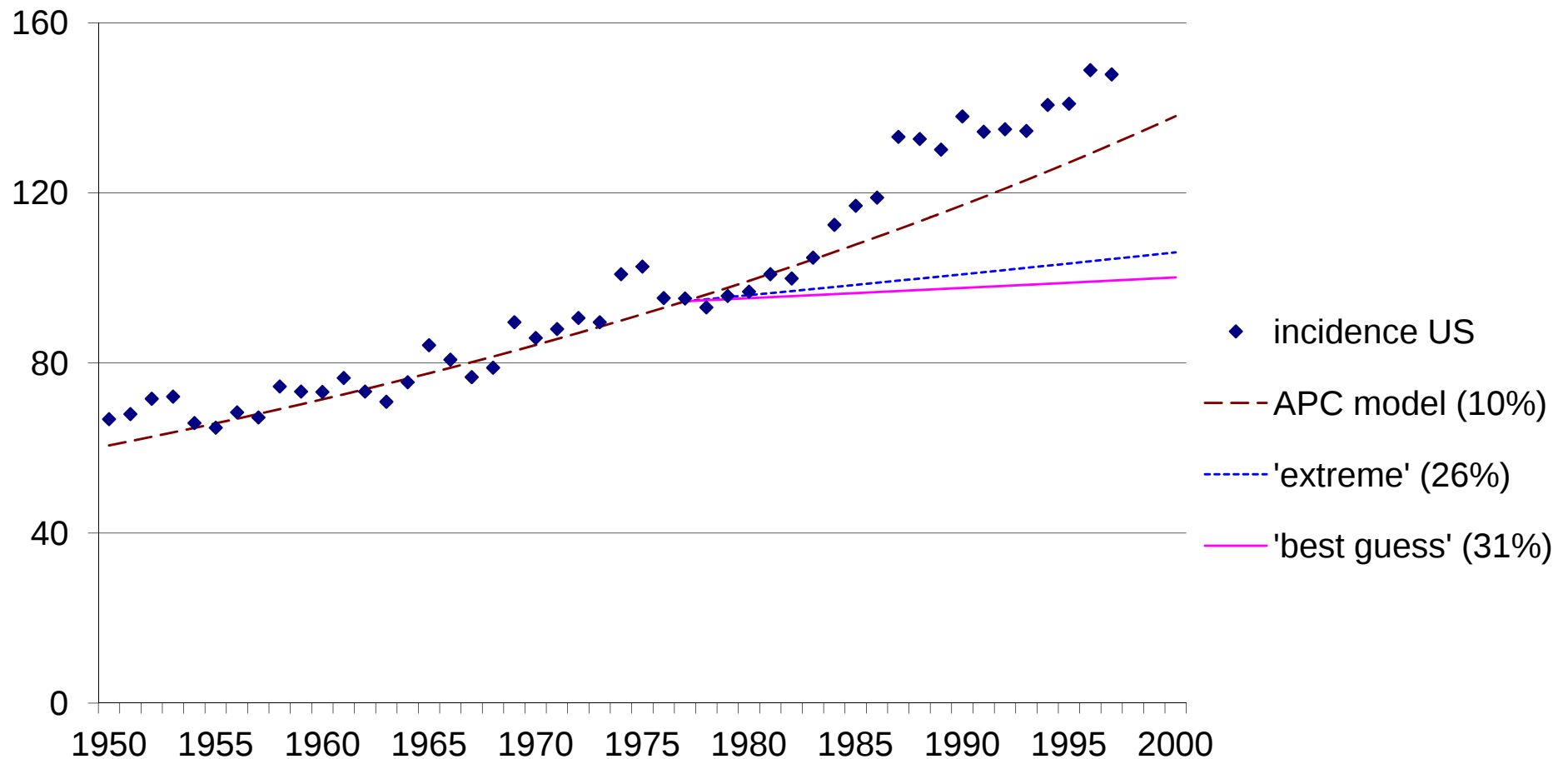
Underlying breast cancer risk



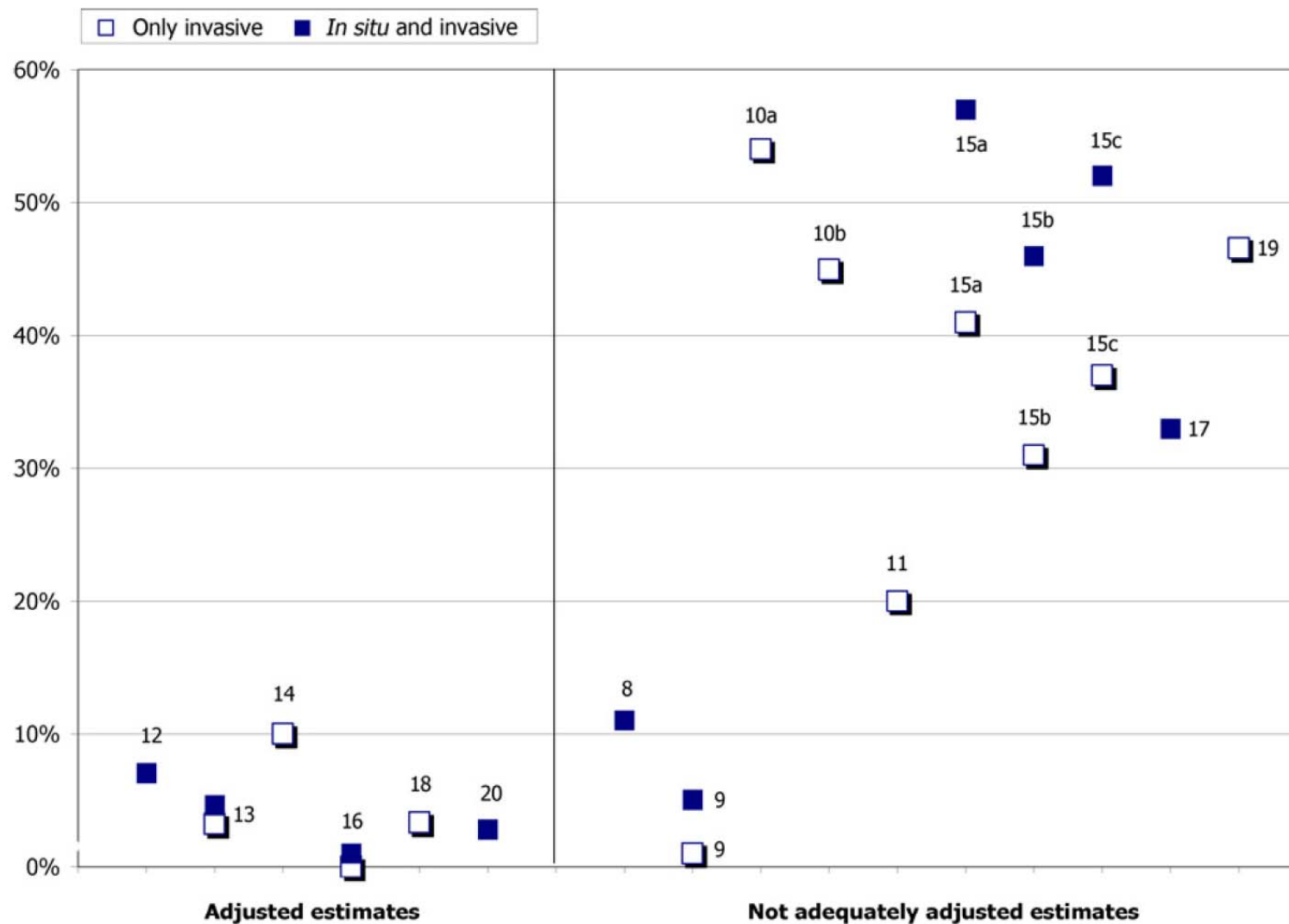
Underlying breast cancer risk



Underlying breast cancer risk



Estimating over-diagnosis



UNCERTAINTY: Epidemiology

Survival rate misleading
for screening
effectiveness

UNCERTAINTY: Epidemiology

Determining true
improvement in
outcome involves
modeling

UNCERTAINTY: Epidemiology

Modeling introduces
uncertainty

In short...

Earliest possible moment to
detect/diagnose/treat cancer might
not be optimal

In short...

We could estimate and deblur due to PSF on average, but not for each pixel

In short...

How do we determine image quality improvement?

In short...

We need to improve image quality in a way that would address where the errors are made most often

In short...

The impact of medical imaging is not always that easy to quantify!



Thanks for listening!

Any Questions?

No?
SUPER!