Biomarkers and the Future of Radiology

John R. Votaw

CBIS 5th Year Anniversary Celebration/Look to the future

February 8, 2013

Statistics/Radiology Collaboration

- The utility of Radiologic procedures must be demonstrated as we move towards an accountable care model for funding healthcare in this country.
- Determination of relevant biomarkers must be followed with demonstrations that they improve patient outcomes.
- Technology is producing imaging data sets that are too vast for any one person to completely explore.
- In 5 years data sets will contain over 100,000 images.
- Efficient methods for extracting the relevant (or discarding the irrelevant) information are needed.

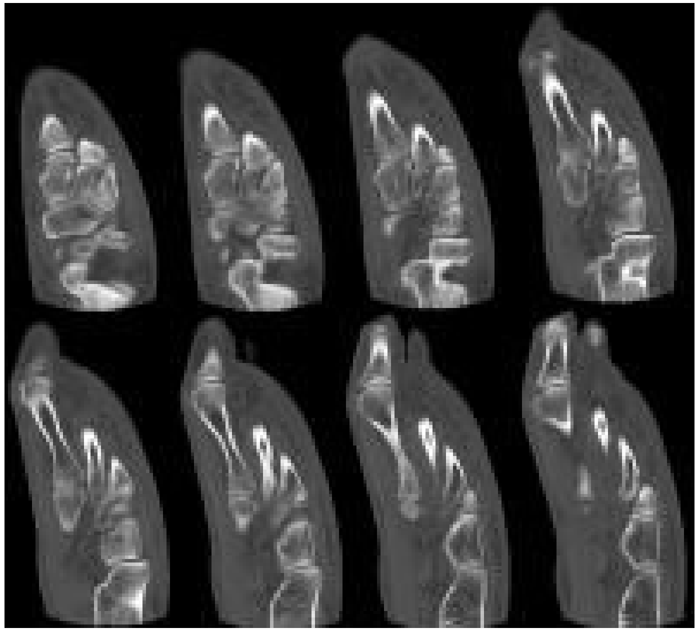
Risk of not performing imaging

- FDG in Non-Small-Cell Lung Cancer
  - Conventional: 81% thoracotomy (78/97), 41% futile (39/78) (Van Tinteren et al. 2002)
  - With FDG: 65% thoracotomy (60/92), 21% futile (19/60)
  - Surgical-related mortality: 6.5%
  - 175k new lung cancer/yr
  - Surgery deaths without FDG: 3766
  - Surgery deaths with FDG: 1574
  - LNT radiation dose: 61 deaths ???
  - Net benefit with PET: 2131

New/Better Biomarkers

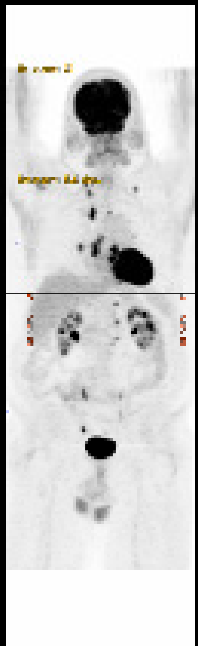
- With FDG: 65% thoracotomy (60/92), 21% futile (19/60)
- Current: Physician examine data with crude machine support (MIP)
- Future: Machine/human partnership
  - Integration of multiple data sets from multiple modalities and multiple sources

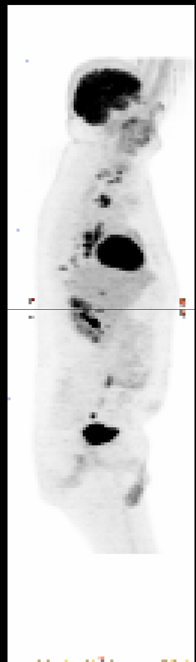

CRFASTTRACK
Ex: B2156570
AP
Se: 3/3
Im: 2/1
FOOT
L
[redacted]
2009 Apr 26
Acq Tm: 16:25:20
Lin:DCM / Lin:DCM / Id:ID
W:4095 L:2047

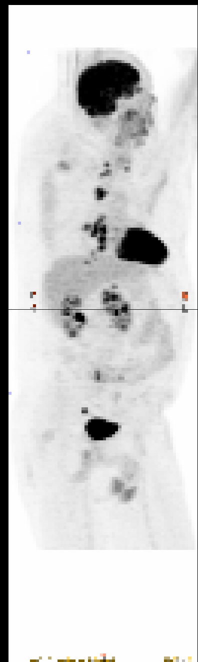


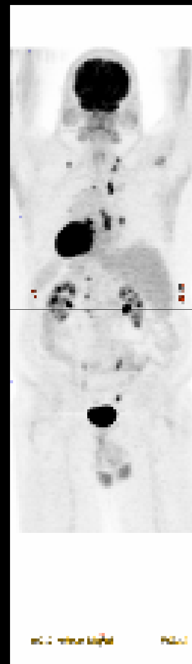

A
H

PET CT
Projection images
(source images = 273)

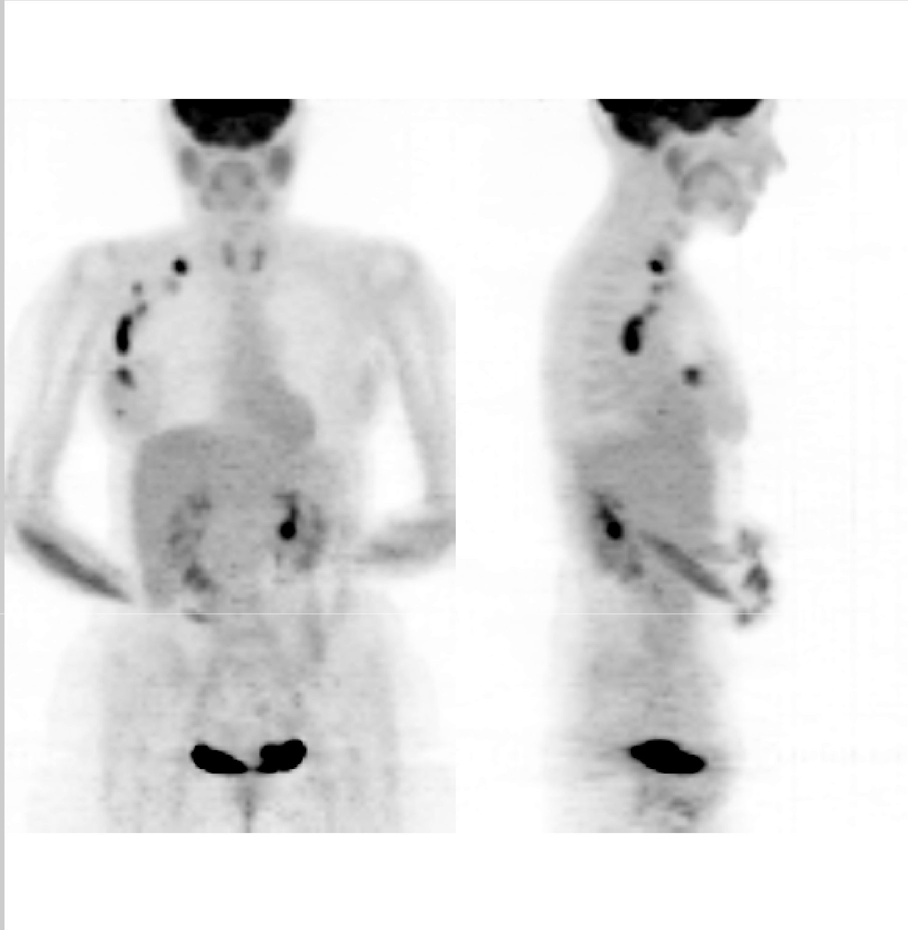








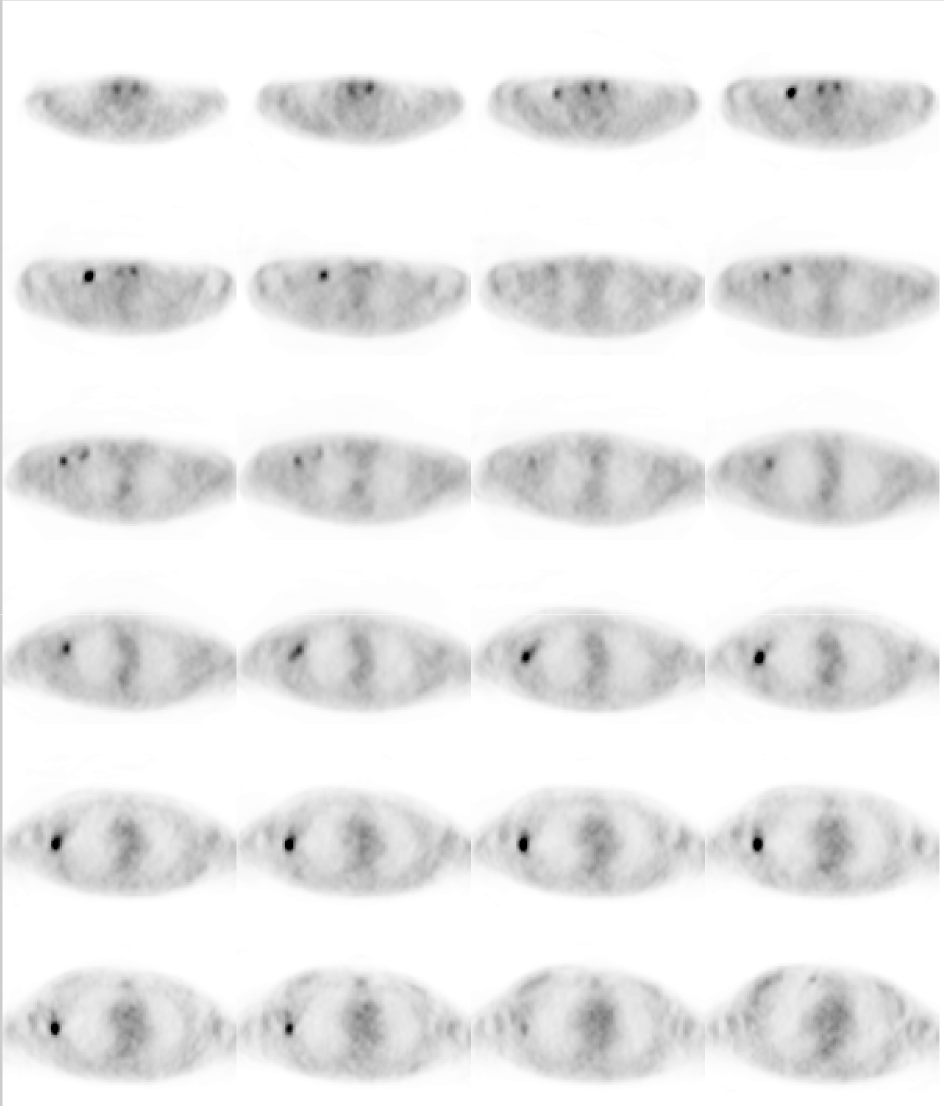
Breast Cancer Missed by Mammography



44 y/o female complained of right breast fullness and slight discomfort from an axillary nodule for several months.

An initial mammogram was performed and called negative. Over the course of the next 6 months, another 2 mammograms were performed. Both were negative.

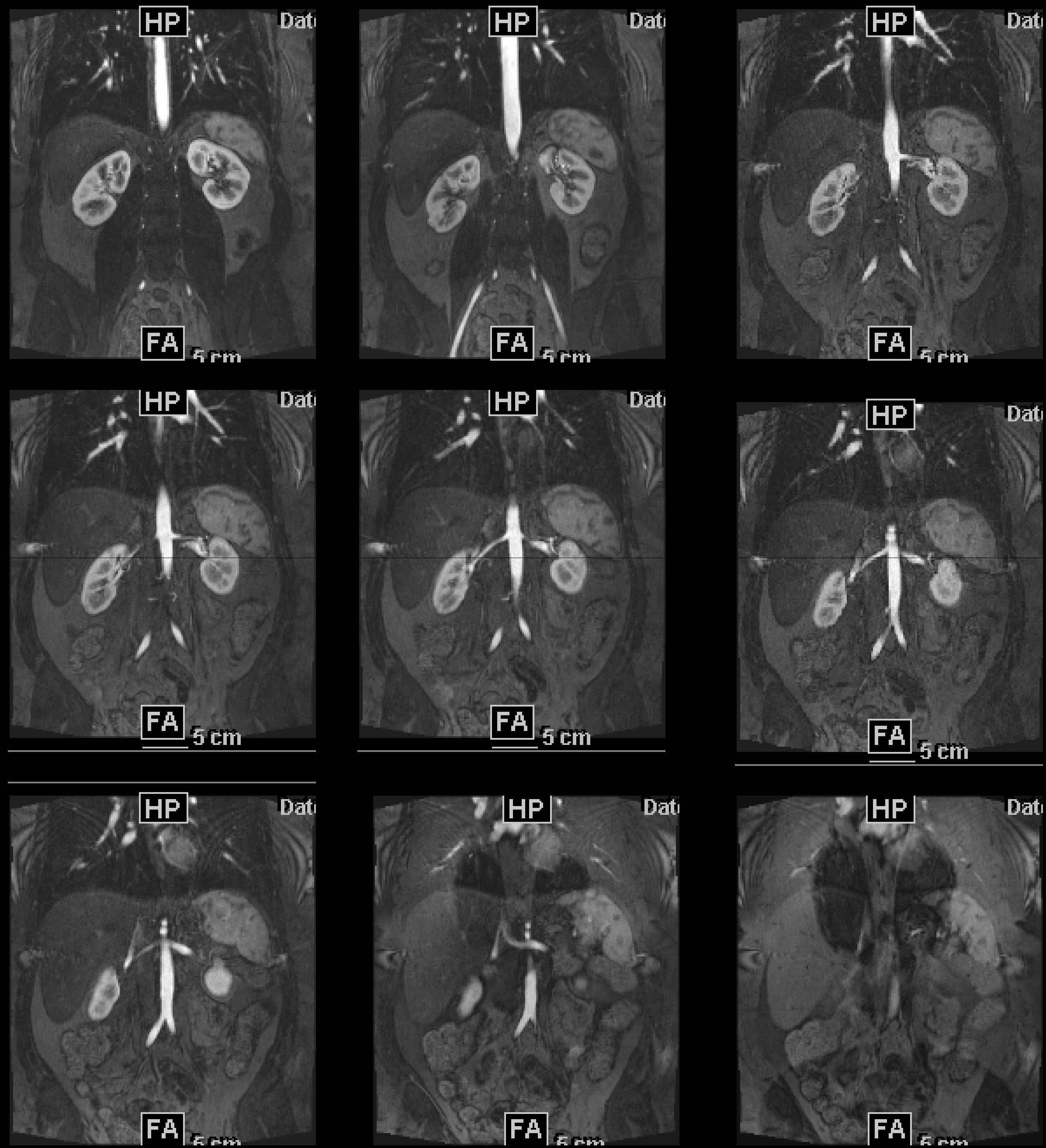
A fine needle biopsy of the axillary node was finally performed which demonstrated poorly differentiated adenocarcinoma. An ultrasound guided biopsy of an 8mm breast nodule was negative.



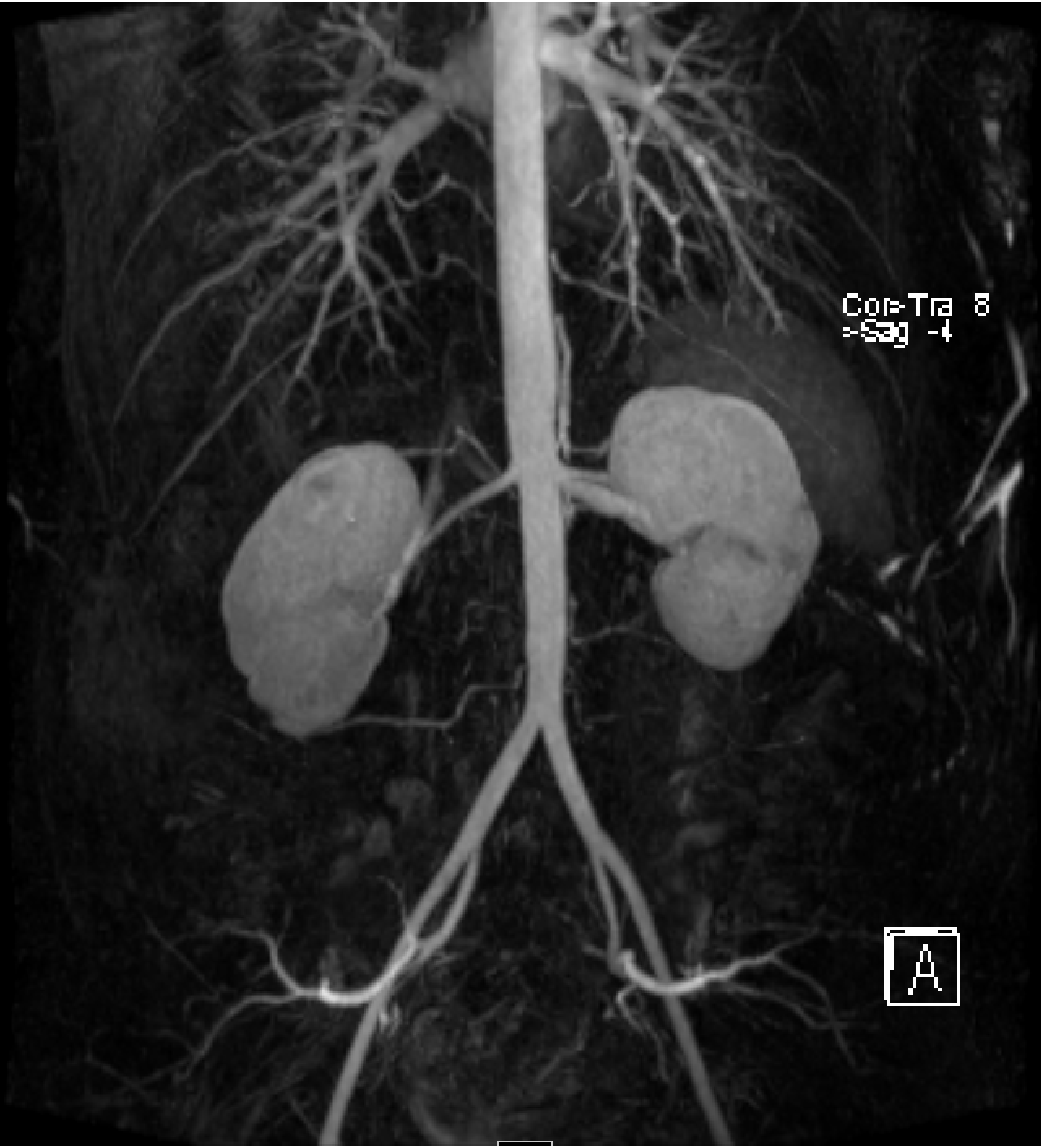
Transverse

The PET scan demonstrates the primary breast cancer and multiple metastatic tumors.

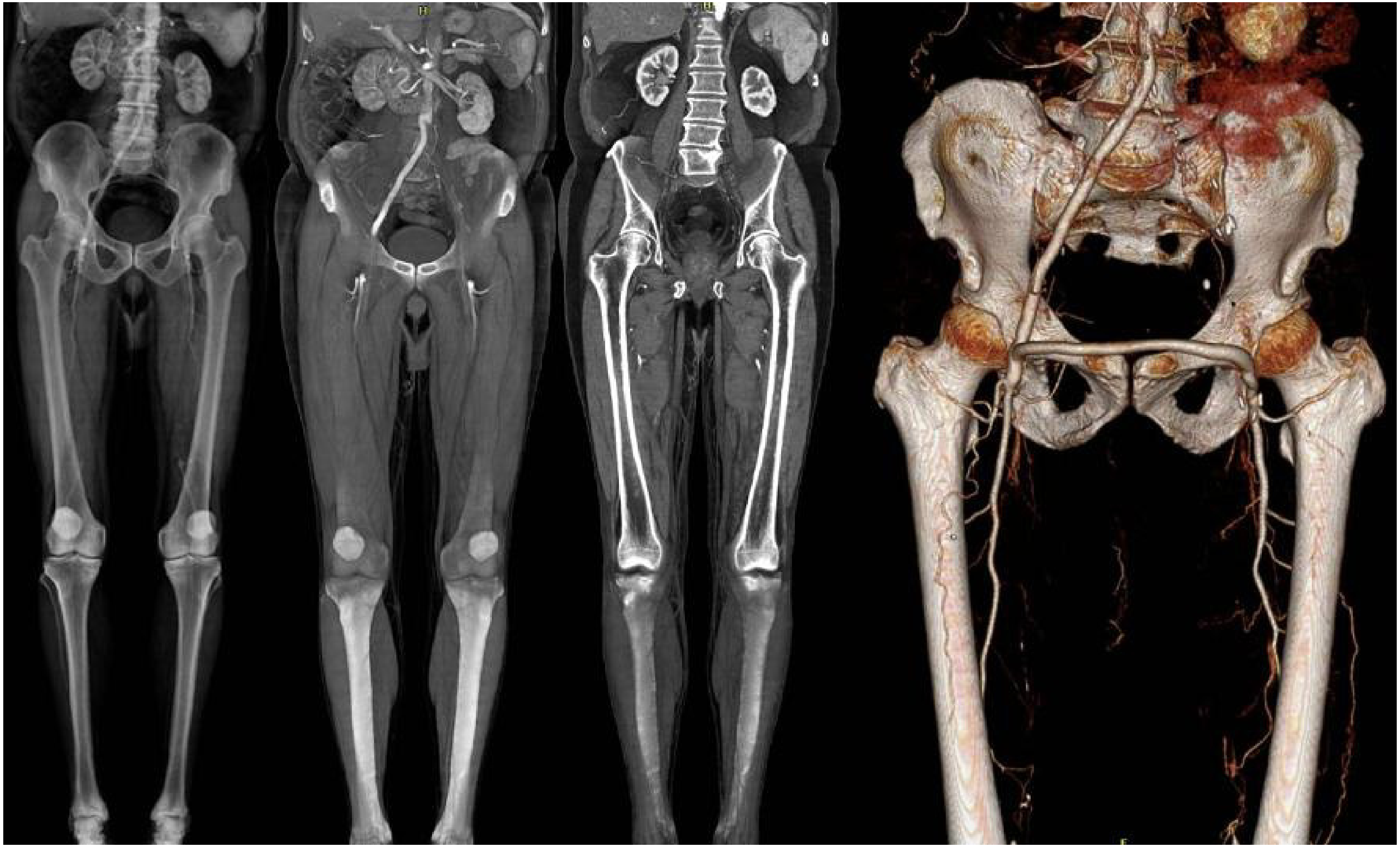
Source images
(88 images)



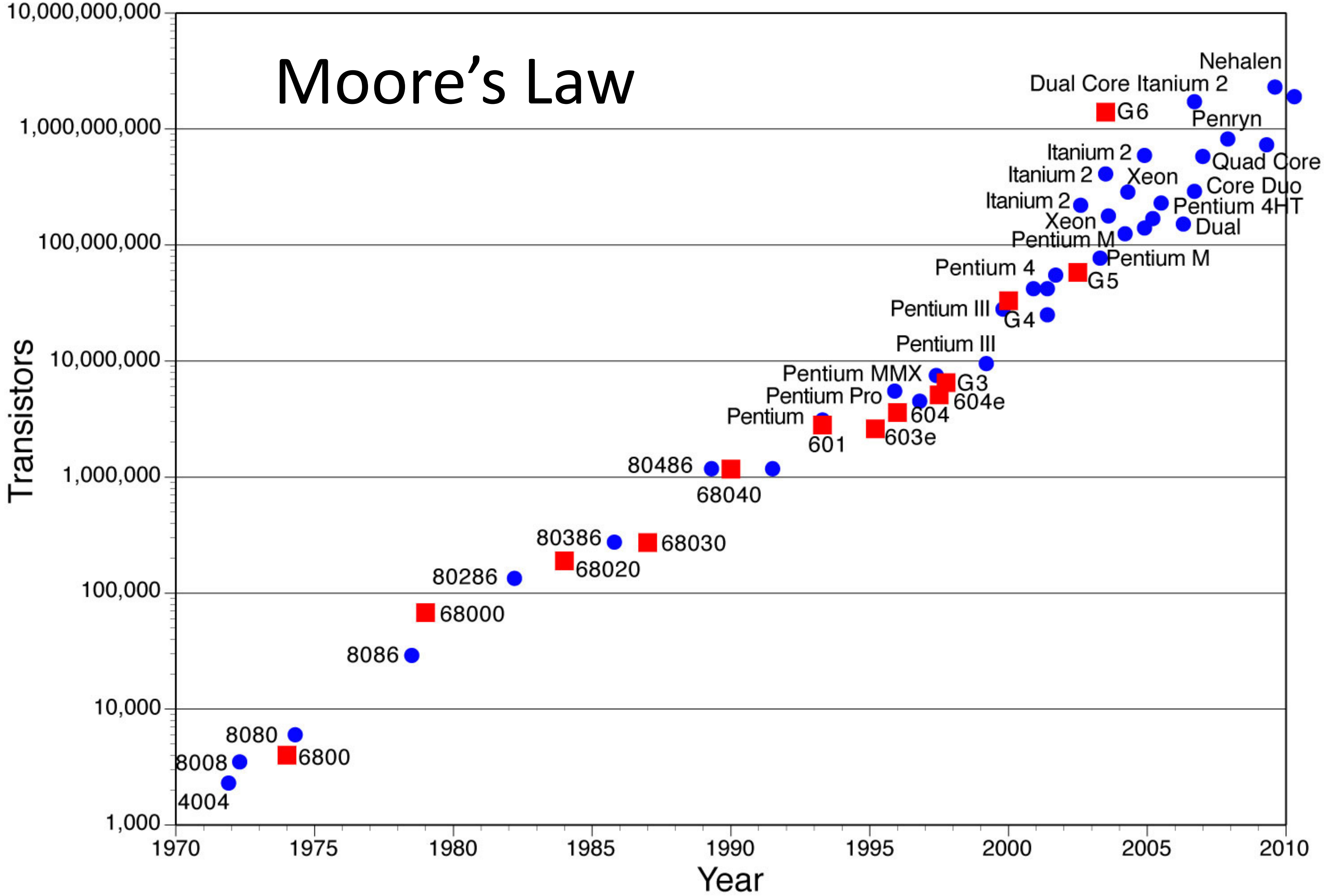
MIP
Abdominal
Angiogram



1792 slices… or 1 volume?



Moore's Law



Transistors
Year
10,000,000,000
1,000,000,000
100,000,000
10,000,000
1,000,000
100,000
10,000
1,000
1970
1975
1980
1985
1990
1995
2000
2005
2010
4004
8008
8080
6800
8086
68000
80286
68020
80386
68030
80486
68040
Pentium
601
603e
604
Pentium Pro
Pentium MMX
604e
G3
Pentium III
Pentium III
G4
Pentium 4
G5
Pentium M
Pentium M
Xeon
Itanium 2
Itanium 2
Itanium 2
Xeon
G6
Dual Core Itanium 2
Nehalen
Penryn
Quad Core
Core Duo
Pentium 4HT
Dual

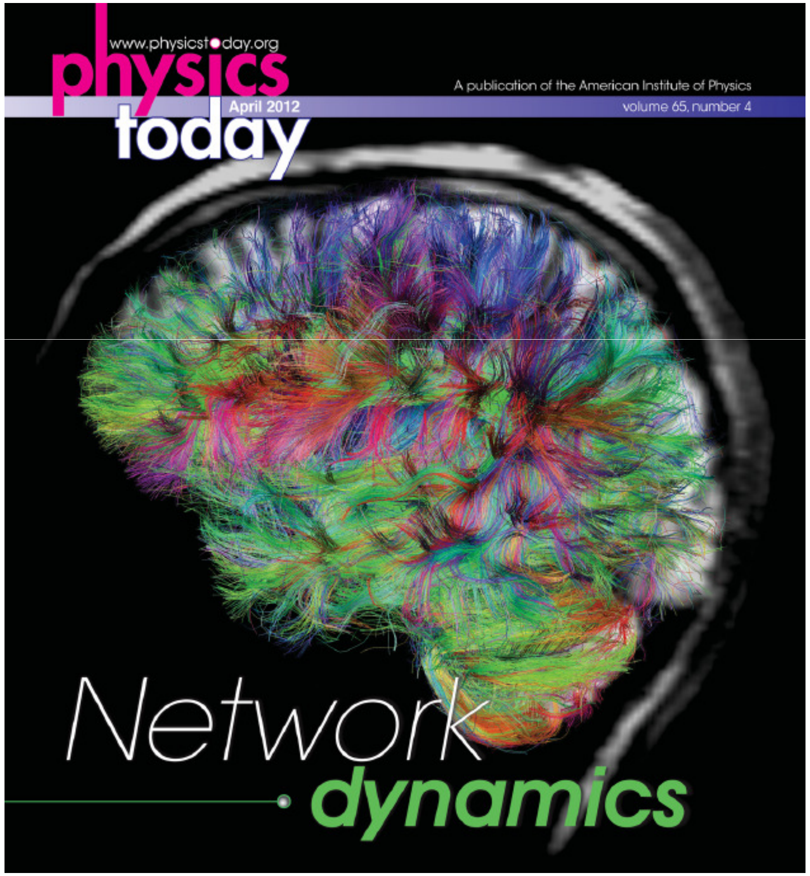
History of Radiology

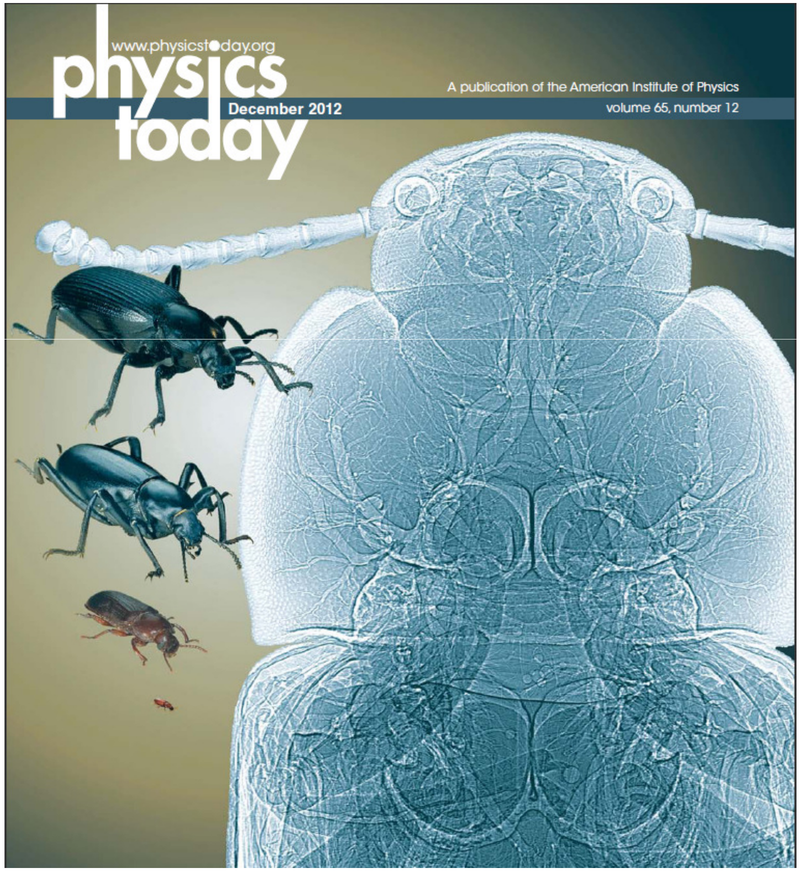
- Planar x-ray 1896
- Multiple views (film)
- 1960 tomography
- Ultrasound 1960
- 1970 CT
- 1980 MRI
- 1974 - 1plane
- 1985 - 5 planes
- 1993 - 31 planes
- 2000 - 207 planes
- Current - 10,000+

- 1 radiologist
- Subspecialization
- Convenience combined modalities (PET/CT)
- Wide-spread data integration

Increasing Size and Complexity of Datasets

- Standard exams performed with faster acquisitions at higher resolution = more data
- Increasing variety of techniques:
  - Perfusion
  - Diffusion
  - Arterial spin labeling
  - Spectroscopy
  - Elastography
  - Blood volume
  - Mean transit time
  - …

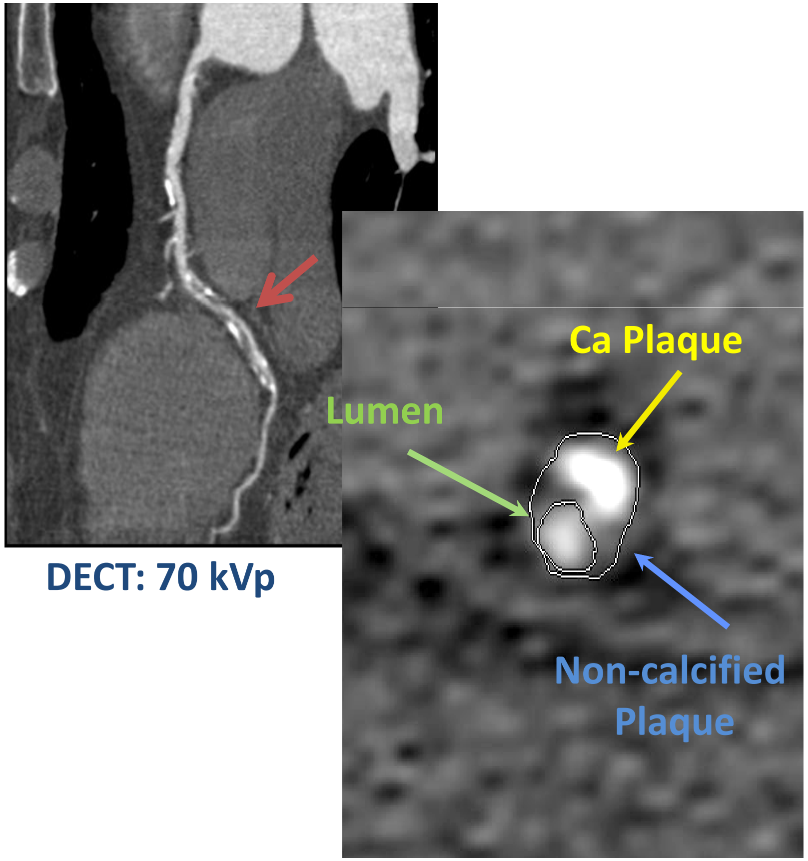

www.physicstoday.org
physics today
A publication of the American Institute of Physics
April 2012
volume 65, number 4
Network dynamics


www.physicstoday.org
physics today
A publication of the American Institute of Physics
December 2012
volume 65, number 12

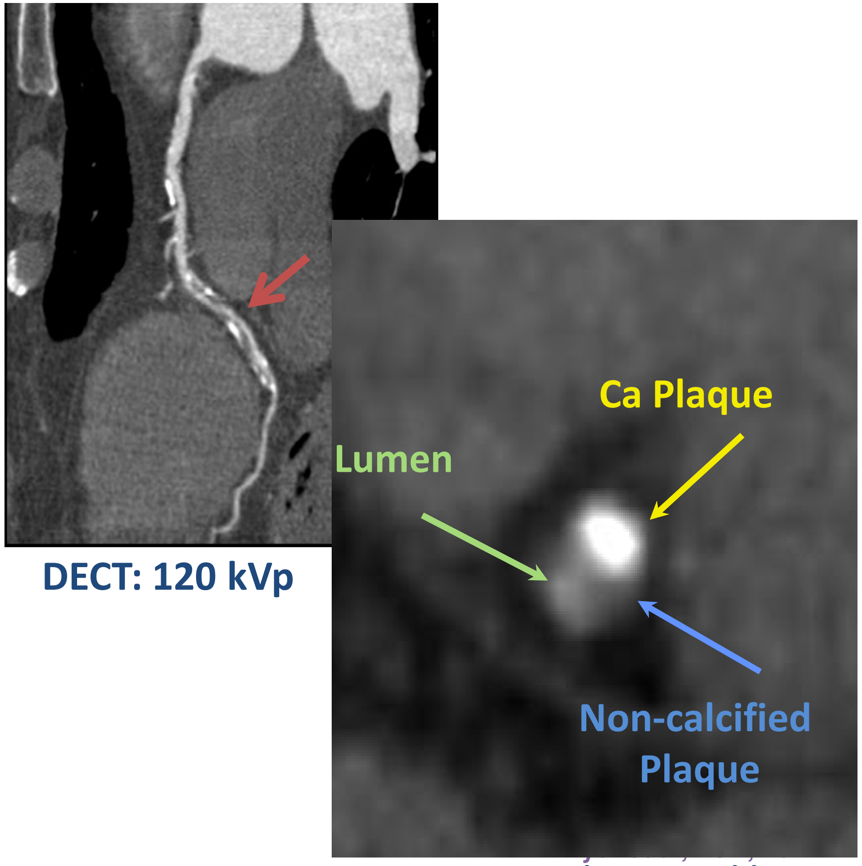
1 mm 250 µm

Vulnerable plaque – A clinical challenge (I)

State-of-the-art dual energy CT in the clinic is capable of material decomposition, but needs higher spatial resolution



DECT: 70 kVp



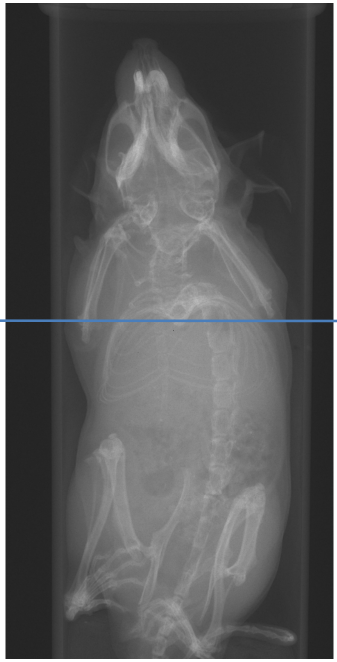
DECT: 120 kVp

Courtesy: Dutta, PhD, GE Healthcare

X-ray differential phase contrast CT (DPC-CT)

Preclinical: Pathophysiologic, pharmacologic and therapeutic research in cancer, athrosclerosis, …

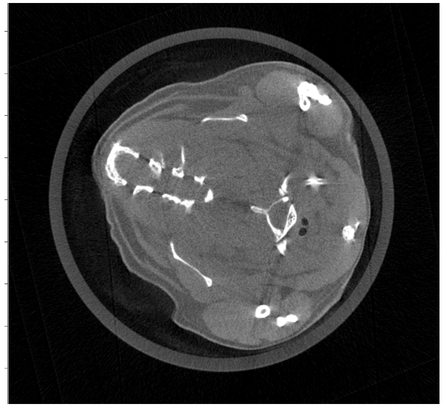
Clinical: Breast imaging …



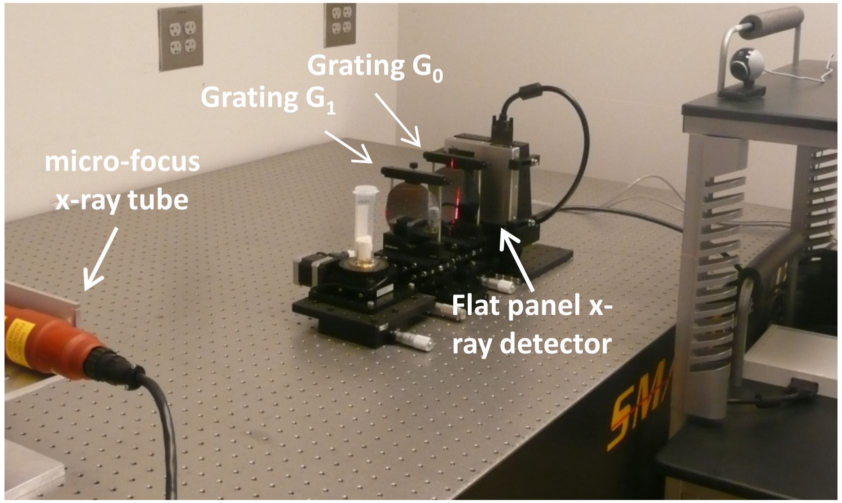
Projection image

Phase contrast

coming soon



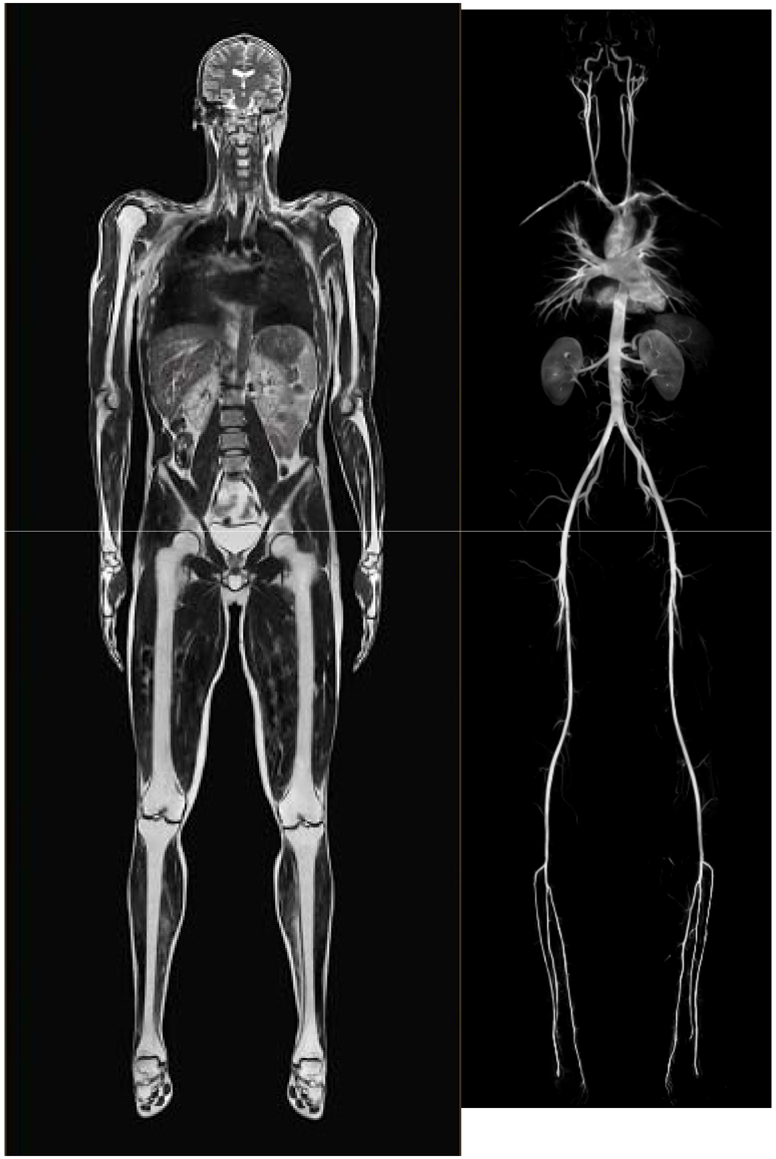
Attenuation contrast



Prototype phase/attenuation contrast (2-in-1) micro-CT

Xiangyang Tang Lab

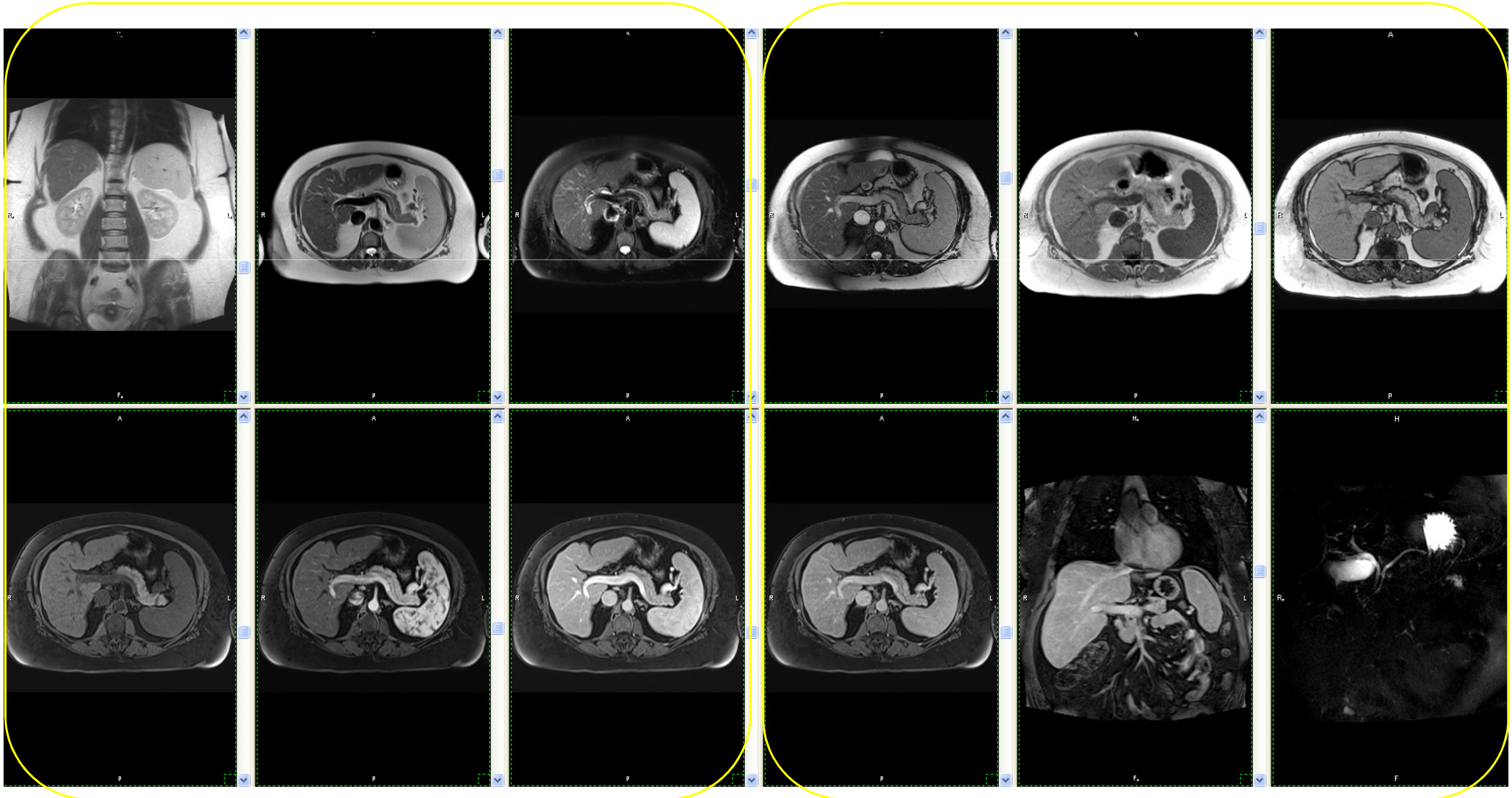
MRI – Large Datasets



Whole Body MRI

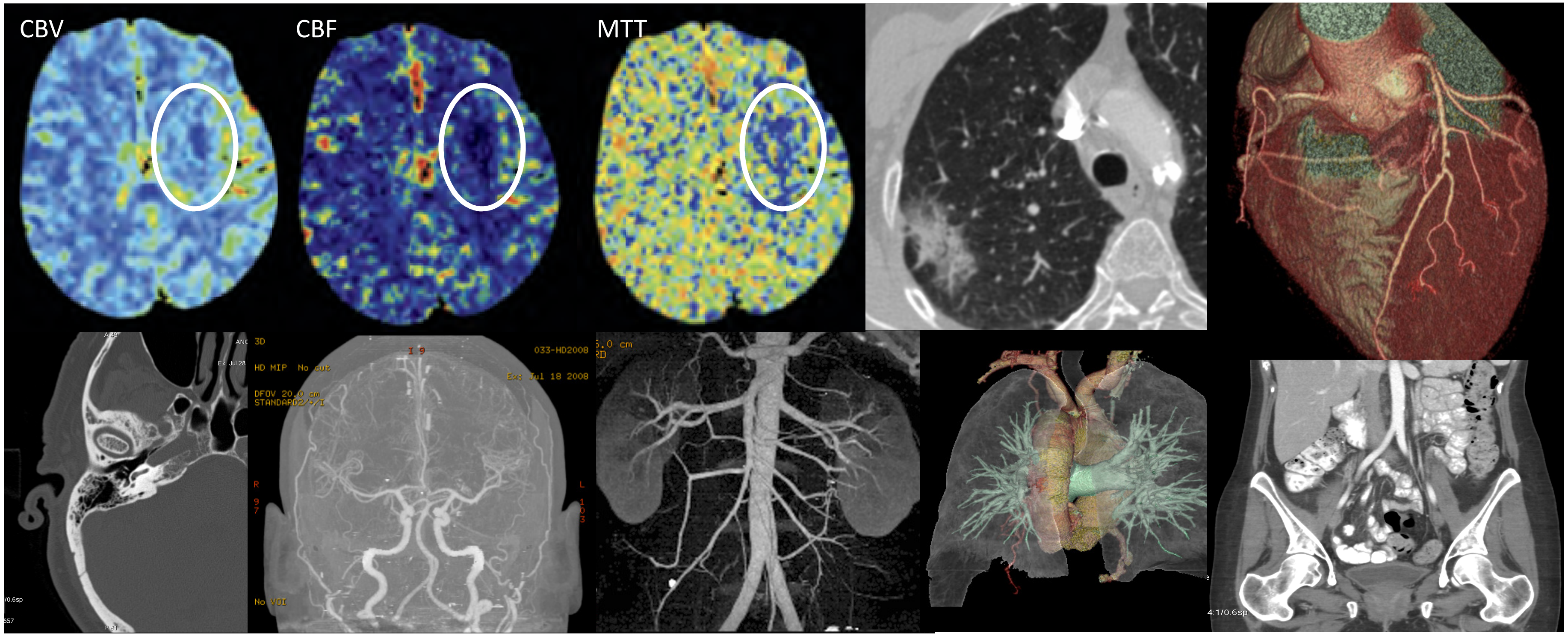
Comprehensive Internal Medical Exam and "The Virtual Biopsy"

MRI Sequences ≈ Histology Stains



The most common clinical applications of CT

- **Cardiovascular:** stenosis, plaque, stent …
- **Body:** chest, abdomen, pelvis
- **Head & Neck:** trauma, stroke, brain, carotids …
- **Misc:** extremities, interventional, …




IBM
11
IBM
10


1997


IBM
POWER7


THINK
$2,400
$31,881
$5,400
Ken
WATSON
BRAD

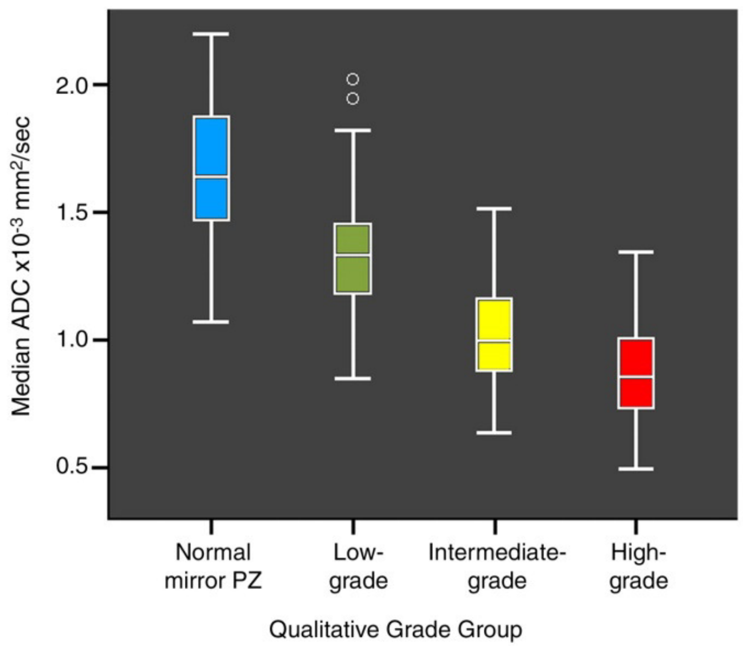

Who is Stoker?
(I FOR ONE WELCOME OUR NEW COMPUTER OVERLORDS)

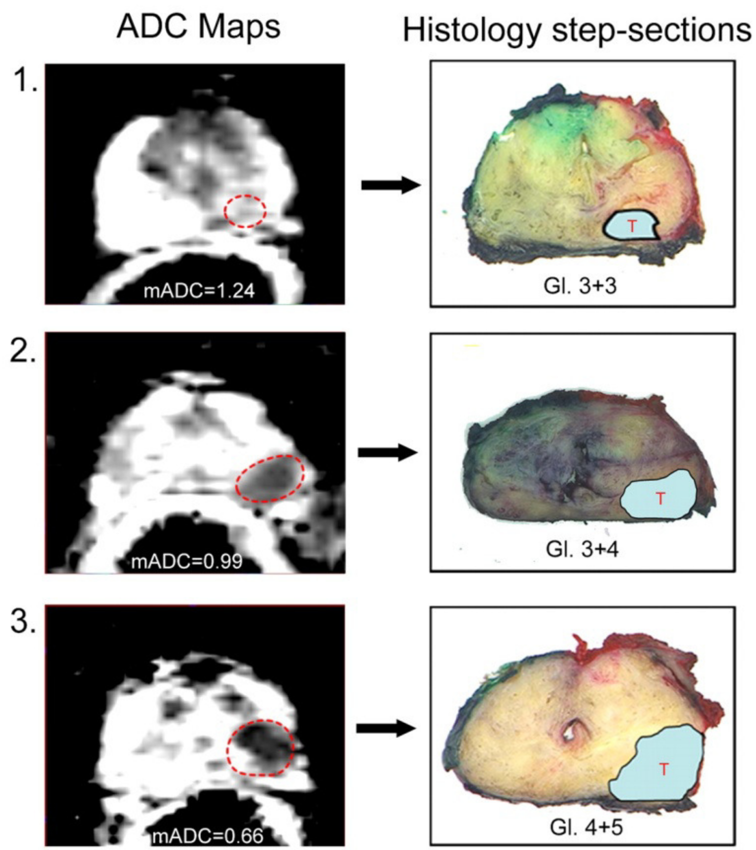
Quantitation

- Radiology
  - Calculate values for parameters known to be physiologically important
- Statistics
  - When are these parameters abnormal?
  - Do the data sets contain other parameters or combination of parameters that are specific for disease?

DWI vs Gleason Score

- Hambrock et al Radiology 2011
  - n=51 PZ cancer
  - Difference between median ADCs of LG and IG larger than that between IG and HG.
  - A_z of 0.90 for median ADC to differentia LG from combined IG and HG



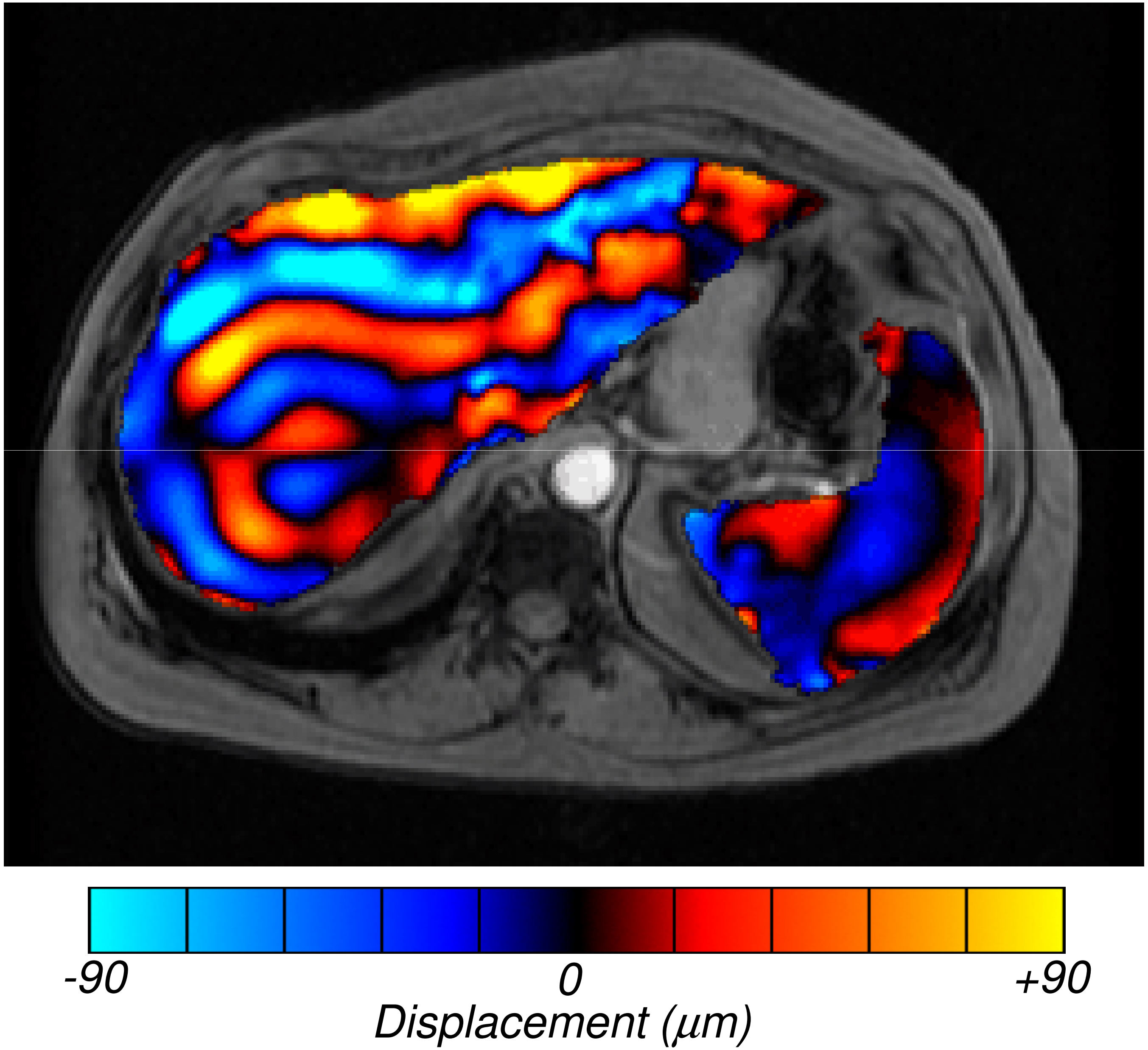


Elastography

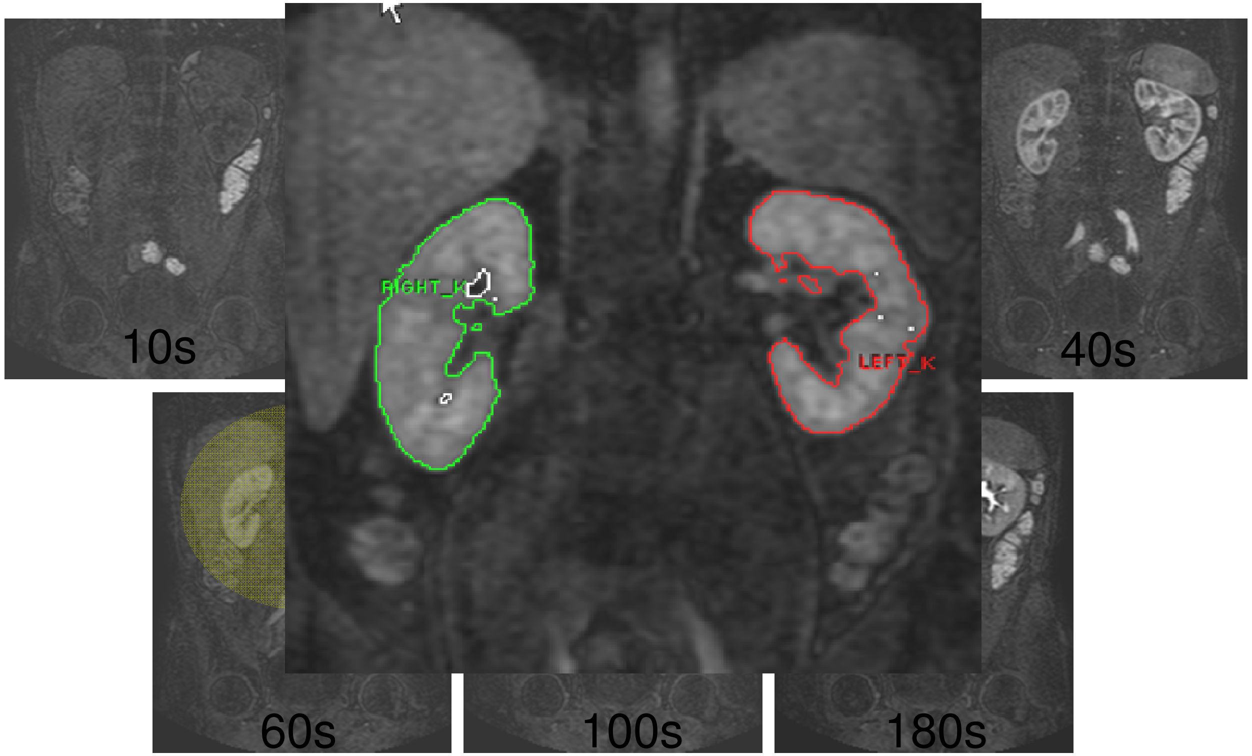
Tumors are 5-28 times stiffer than normal soft tissue

Fibrosis score and elasticity are correlated

Developed by
Richard Ehman
Mayo Clinic

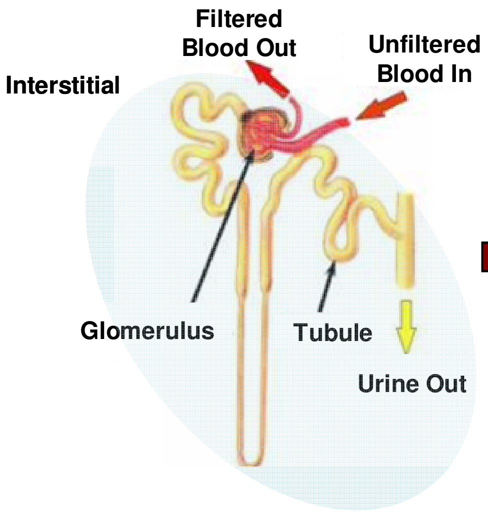


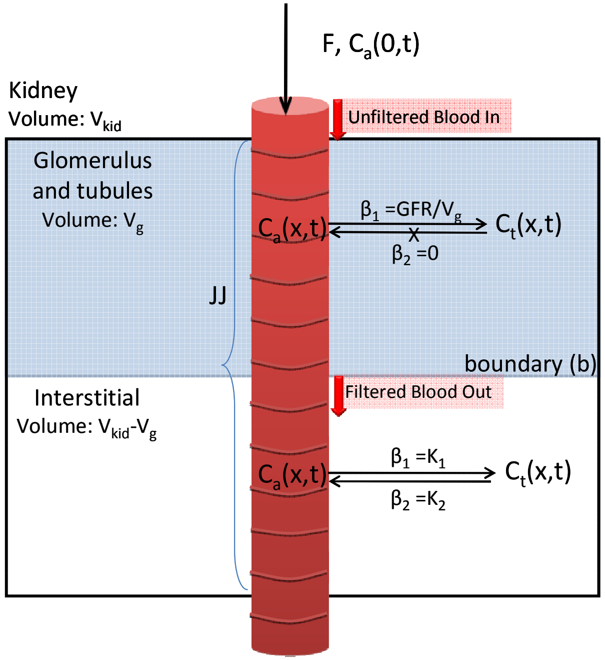
MRNU



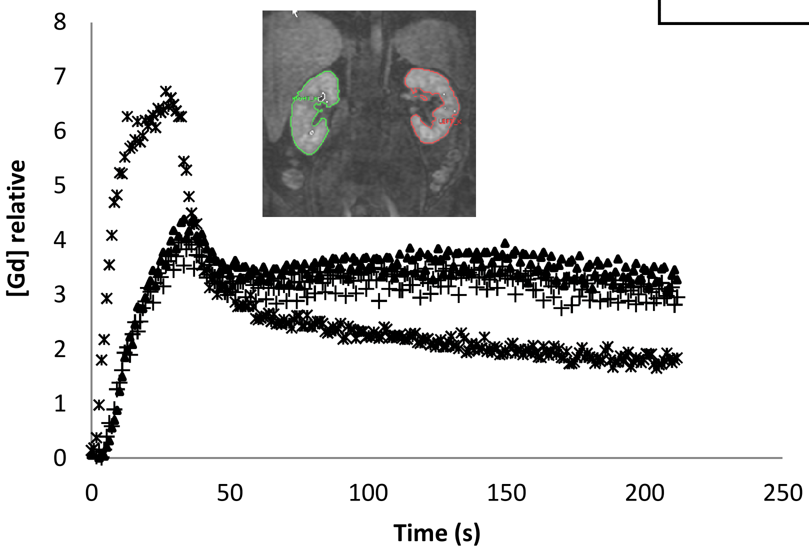
Circumscribed ROI's on cortical-medullary phase image just prior to contrast excretion into the pelvis

Relative signal values = (St – So) / So

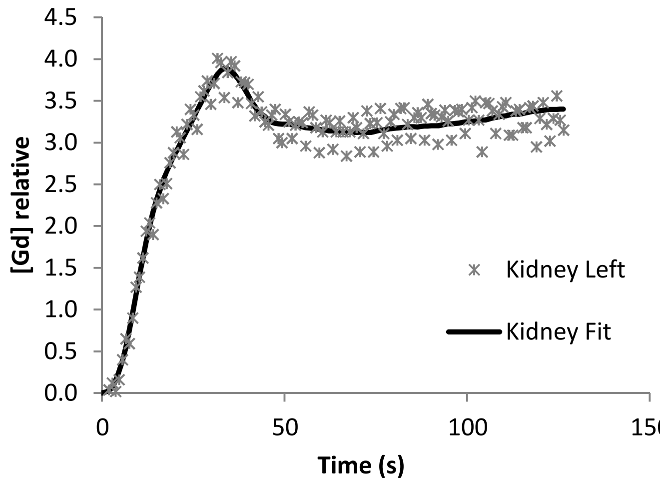




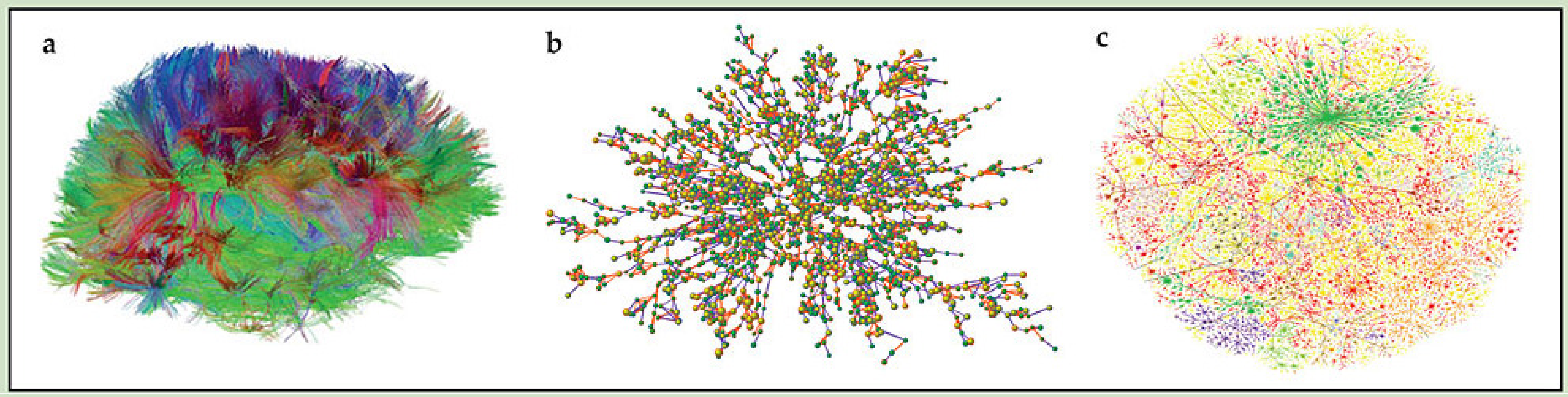
(Left) Illustration of a nephron
(Right) Equivalent mathematical model

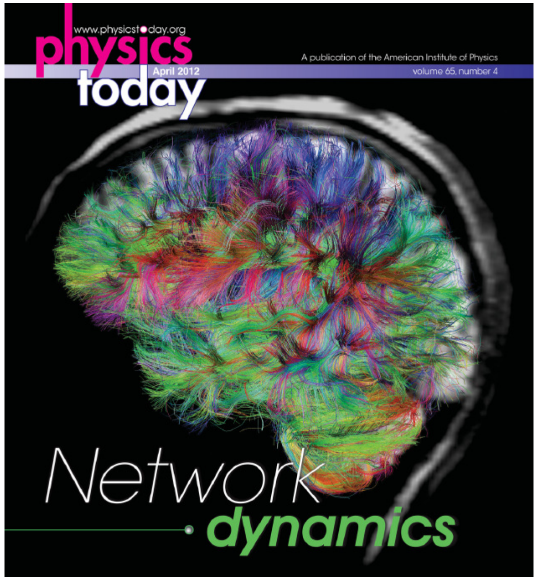


Gd concentration in the aorta and kidneys over time are derived from circumscribed ROIs



Fitting the model to the kidney data gives estimates of GFR and RBF





Motter and Albert, Physics Today April 2012 p 43

Eigenvalue Concept

I1	I2	I3	I4	I5	…	N
P1	P1	P1	P1	P1	…	P1
P2	P2	P2	P2	P2	…	P2
P3	P3	P3	P3	P3	…	P3
P4	P4	P4	P4	P4	…	P4
P5	P5	P5	P5	P5	…	P5
.	.	.	.	.	…	.
.	.	.	.	.	…	.
.	.	.	.	.	…	.

V1	V2	V3	V4	V5	…	N
v1	v1	v1	v1	v1	…	v1
v2	v2	v2	v2	v2	…	v2
v3	v3	v3	v3	v3	…	v3
v4	v4	v4	v4	v4	…	v4
v5	v5	v5	v5	v5	…	v5
.	.	.	.	.	…	.
.	.	.	.	.	…	.
.	.	.	.	.	…	.

$\lambda 1 > \lambda 2 > \lambda 3 > \lambda 4 > \lambda 5 > \ldots > \lambda N$

"Important Information"

(Biomarkers)

Noise

Summary

- Information content exploding
  - Finer detail images
  - Multi-modality
  - Many different properties (transmission, stiffness, light speed, density, metabolic rates, …)
- Find relevant information
- Find unexpected information
- Need Human-Machine (decision making) interaction
  - Point out “high probability” areas
  - Remove “low probability” areas
- Transmit information to users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