Advanced Medical Imaging with Synchrotron and Compton X-ray Sources

Bologna, 21-22 November 2019

Potential applications of ICS in Biomedical imaging

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Is ICS a compact synchrotron?

- YES … because:
  - The size of the facility is smaller
  - The cost of the facility is lower
  - The required flux for biomedical applications is comparable
  - The required monochromaticity is sufficient

- We can basically replicate all the biomedical experiments …

Is ICS a compact synchrotron?

- NO … because:
  - Higher divergence: Field of view allows for 2D imaging
  - Energy of the X-ray beam can be "easily" extended to several hundreds of keVs (ESRF 25-185 keV@ID17)
  - Dual-energy beam is "available" (see BriXs design)
  - Intrinsic monochromaticity (no channel-cut crystal & negligible harmonic contamination)
- What do we really need from a novel high-brilliance and monochromatic x-ray source?

Perspective

Tunable Monochromatic X Rays: A New Paradigm in Medicine

Frank E. Carroll[1,2]

"Among the anticipated uses of monochromatic beams in medicine are markedly improved

Mammography, K-edge imaging, Phase-contrast imaging, Time-of-flight imaging, Small-animal imaging, and Protein crystallography."

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Review paper

K-edge subtraction synchrotron X-ray imaging in bio-medical research

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dose absorbed in water, or 50 µGy/s dose rate. This agrees well with the dose rate reported by Rutt et al. [6]. However, the optical size of the source is much smaller in the present set-up, improving the spatial resolution. The gain of intensity at the detector is about 10-fold, because the beam is not filtered for energy selection.

The above estimates correspond to detection of very small concentrations of the contrast agent in small volume. For a given SNR, the required exposure is inversely proportional to square of the contrast agent density and the object thickness. If the spatial and contrast resolution can be reduced, the exposure time may be decreased in quadrature. The rotating anode X-ray tube is a pulsed source, and the exposure rate is probably 10–100 Hz. The frame rate of a pixel detector is about 10 times larger (Pilatus3 X CdTe, Dectris Ltd) [115] so that successive projection images could be recorded, e.g. to reduce the motion artifacts. It is evident that there is great potential in fluorescence imaging, when optimized instrumentation and image treatment algorithms are developed.

7. Discussion and conclusion

This paper has reviewed the application of K-edge subtraction imaging in the field of biomedical research, and their potential clinical applications as well. The applications have been only to fundamental and applied research programs with no translation to the clinic.

The transvenous coronary angiography programs discussed in detail the small airways of the lung and small vasculature.

The application of K-edge subtraction imaging in the field of biomedical research has clearly benefitted from technological advances in X-ray sources, optics and detectors. The development of synchrotron sources with high flux, high detector resolution and continuous X-ray spectra covering a wide range of K-edge energies of relevant elements, has allowed the development of diverse applications and new imaging modalities. With the advent of new X-ray sources such as compact Compton sources, KES imaging research and potential clinical applications will continue to be important areas of biomedical research.

Funding

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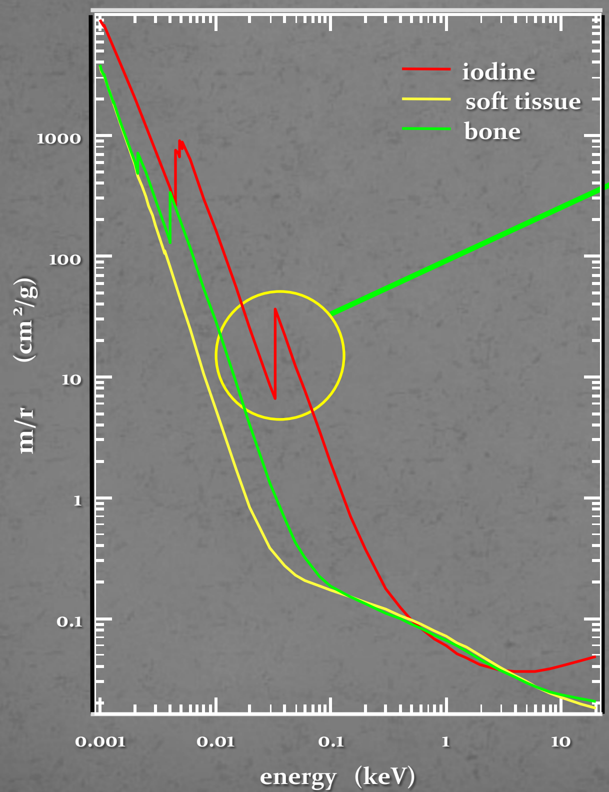
Conflict of interest

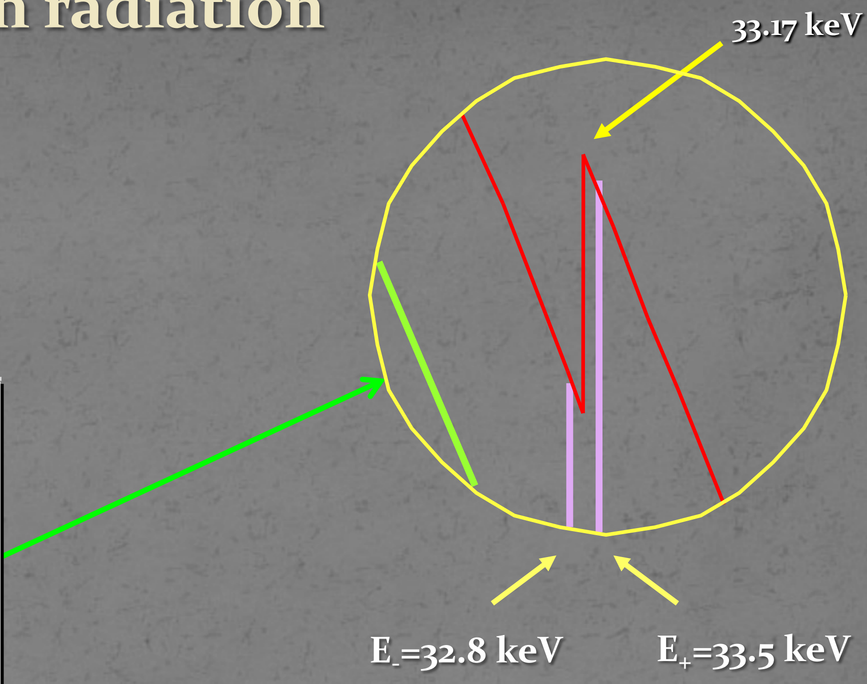
The authors have no relevant conflicts of interest to disclose.

References

[1] Roentgen WC. On a new kind of rays. Science 1895;59(3):227–31.
[2] Mistretta CA, Ort MG, Kelcz F, Cameron JR, Siedband MP, Crummy AB. Absorption

K-edge digital subtraction angiography with synchrotron radiation





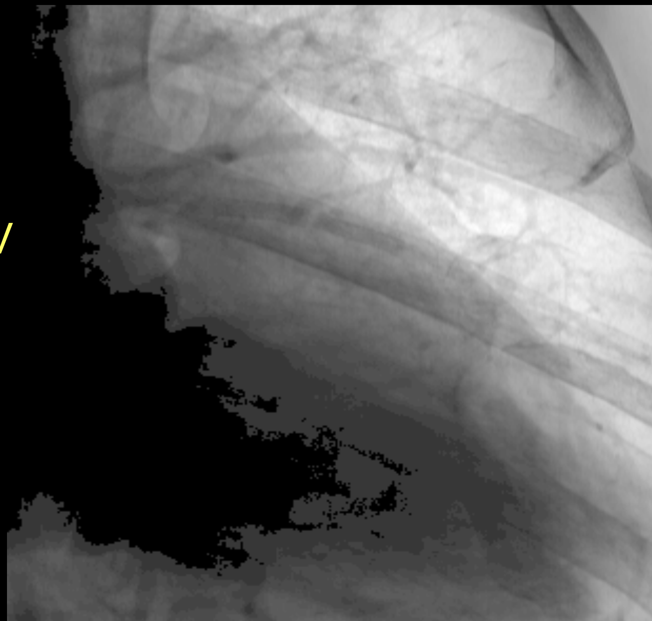
The concentration of the contrast medium in the artery may be reduced.

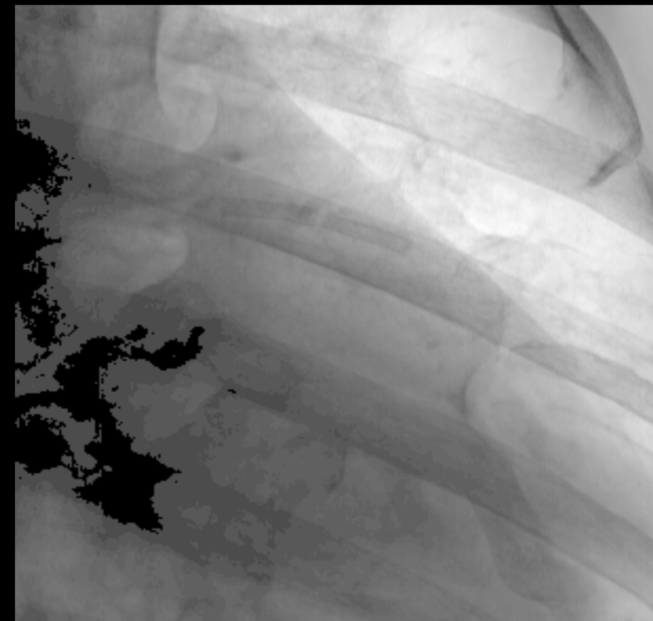
Catheter may be inserted by intravenous injection instead of arterious one.

Iodine and tissue images

Above

$E_+ = 33.5$ keV





Below

$E_- = 32.8$ keV

Contrast

Tissue

Coronary Angiography @ ESRF

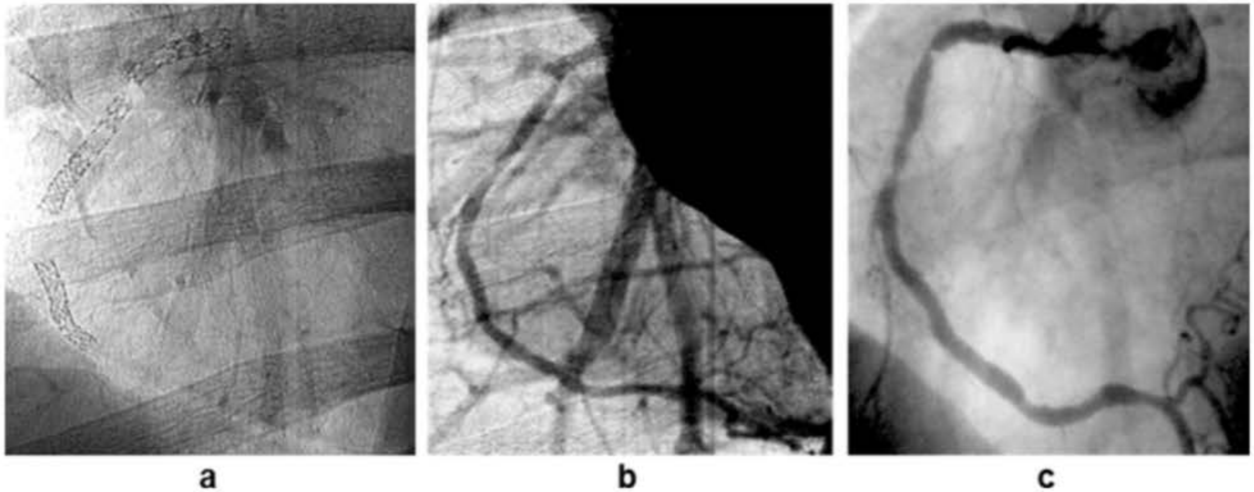


Fig. 8. View of the right coronary artery (RCA) in a patient with stents. The stents are visible in the tissue image (a), the iodine is visible in the subtraction image (b) and the conventional angiography image is shown in (c) [27]. Copyright 2005, with kind permission from Oxford University Press.

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PAPER

Inverse Compton radiation: a novel x-ray source for K-edge subtraction angiography?

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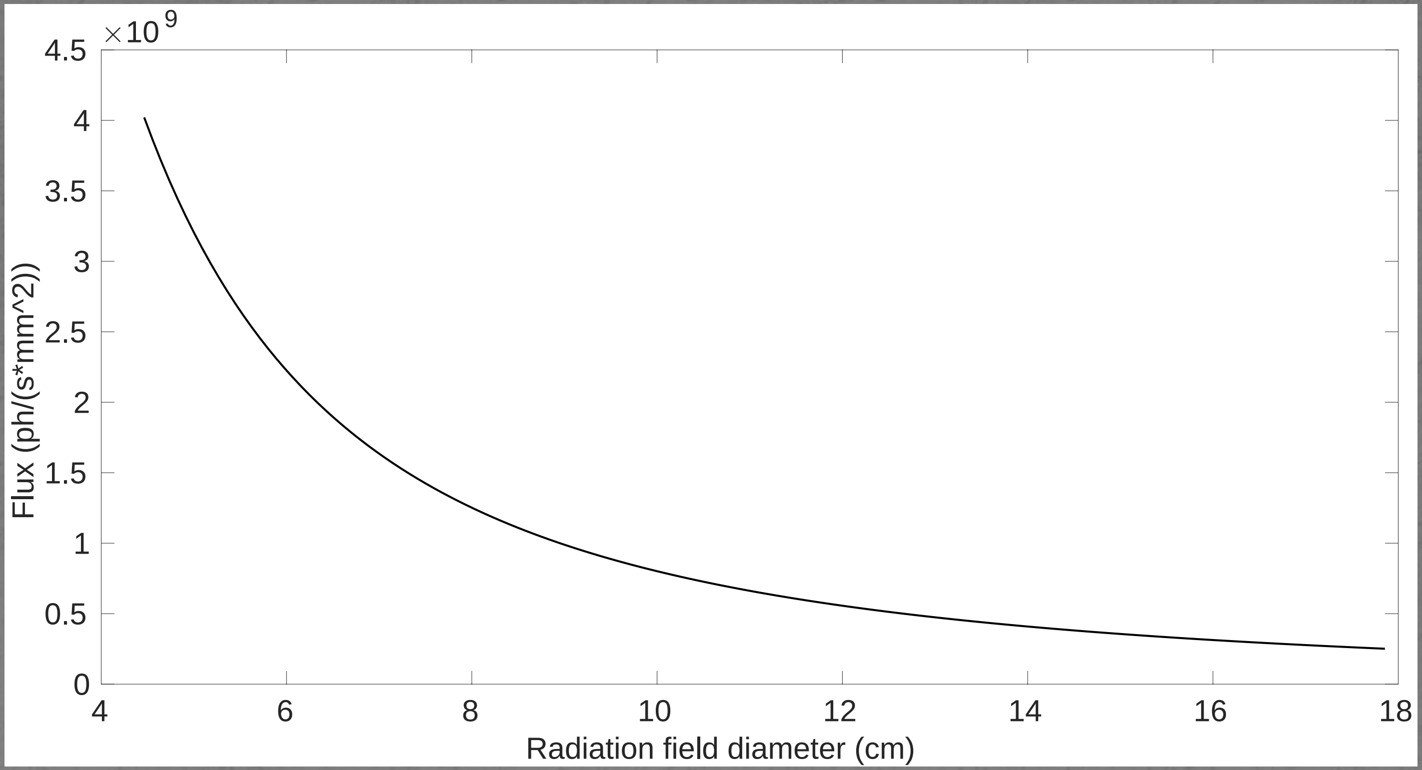
Abstract

Coronary angiography is clinically used worldwide to diagnose diseases of coronary arteries. Despite its effectiveness, this technique is quite invasive and it is associated with significant risks due to the arterial catheterisation needed to inject the contrast agent. A valid alternative is using the K-edge subtraction (KES) method, which is based on the subtraction of two images acquired at energies bracketing the K-edge of the contrast element. The enhanced sensitivity of KES allows the intravenous injection of the contrast agent, thus reducing the risks of catheterisation. This technique can be effectively implemented by using intense and quasi-monochromatic x-ray beams. Synchrotron radiation has been proven to work well for this purpose, but its cost and size prevent a widespread clinical application. Inverse Compton sources are among the most promising innovative sources of intense and quasi-monochromatic x-rays. These sources are intrinsically more compact than those based on synchrotron radiation. In this work, the potential application of inverse Compton radiation to KES angiography is investigated. To this purpose, after a short review of the physics behind the inverse Compton process, an analytical framework is described. The proposed model is based on the application of the KES algorithm to calculate the SNR of details inside a suitable mathematical phantom. That allowed us to identify the characteristics of an inverse Compton source required for KES imaging. In particular, it was estimated that a photon fluence of 10^8 ph mm^{-2} is necessary to detect signals of clinical interest. Novel sources based on inverse Compton promise to achieve this requirement with an acquisition time of few hundreds of ms. This feature, together with compactness, broad two-dimensional radiation field, absence of harmonic contamination and the ability to deliver high photon fluxes also at high energies, makes this kind of sources promising for KES angiography and other diagnostic applications.

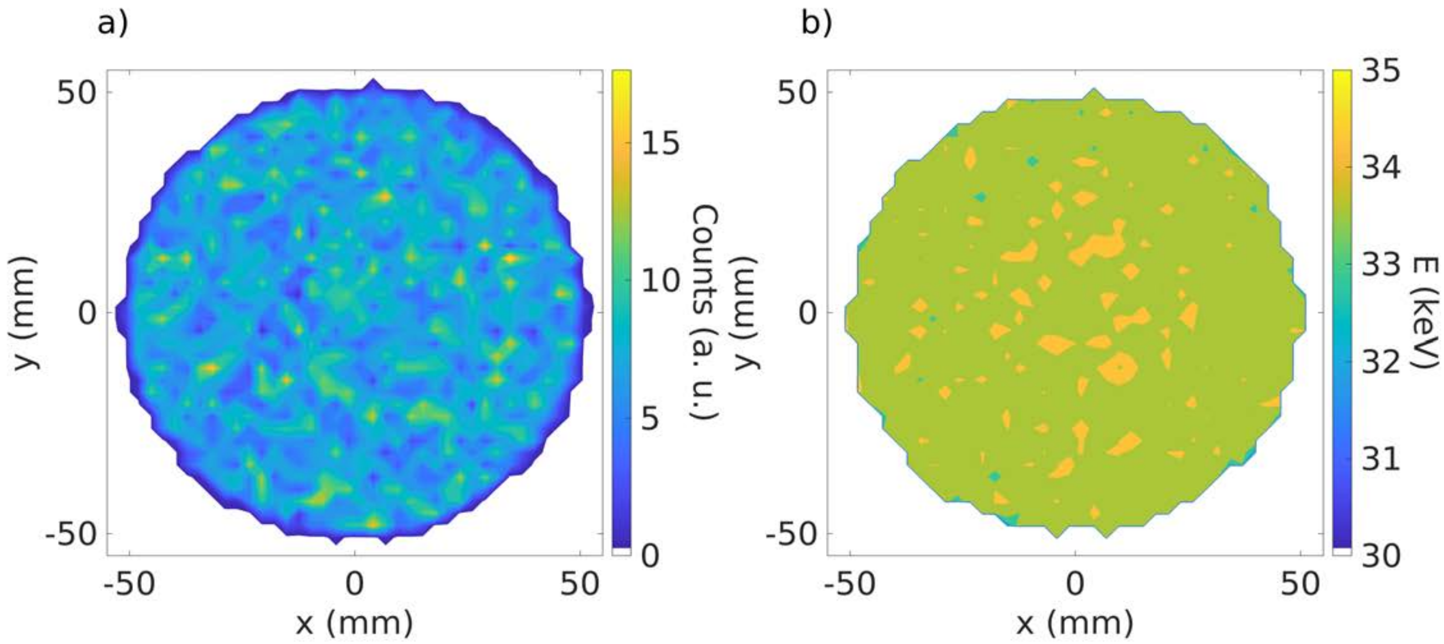
Flux vs irradiation field



For a fixed radiation field size, increasing the bandwidth, and therefore the collimation angle (θ_{max}), leads to:

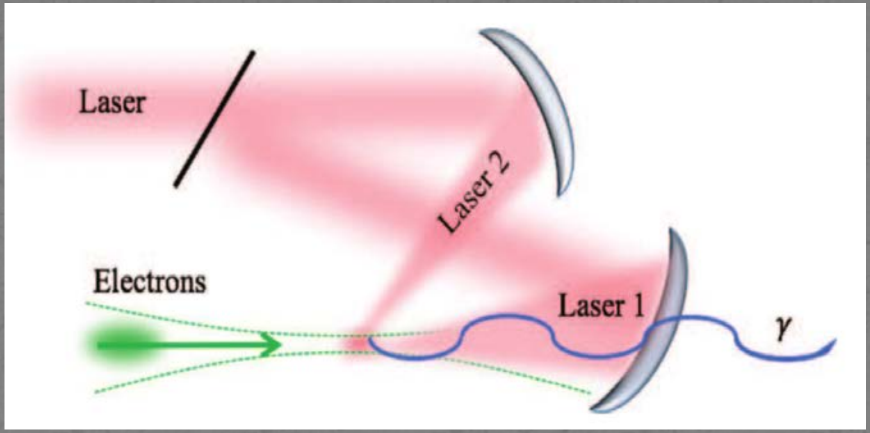
- An increase in the flux (because the distance from the IP is shorter)
- A less uniform radiation field

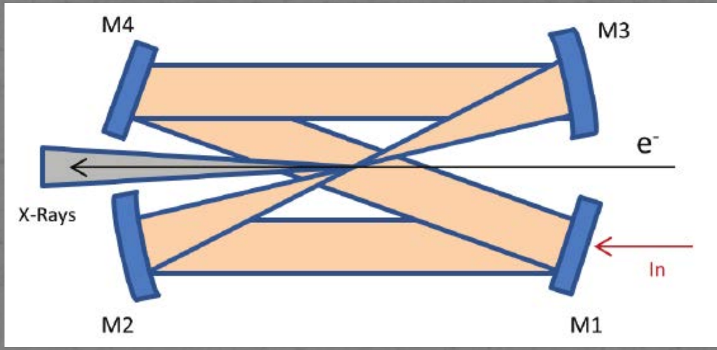
Spatial uniformity of irradiation field



Spatial distribution of a X-ray beam with a mean energy of 34 keV and 1.5% rms BW (θ_{max} = 1 mrad) at 50 m from the IP

Dual-color x-ray beams

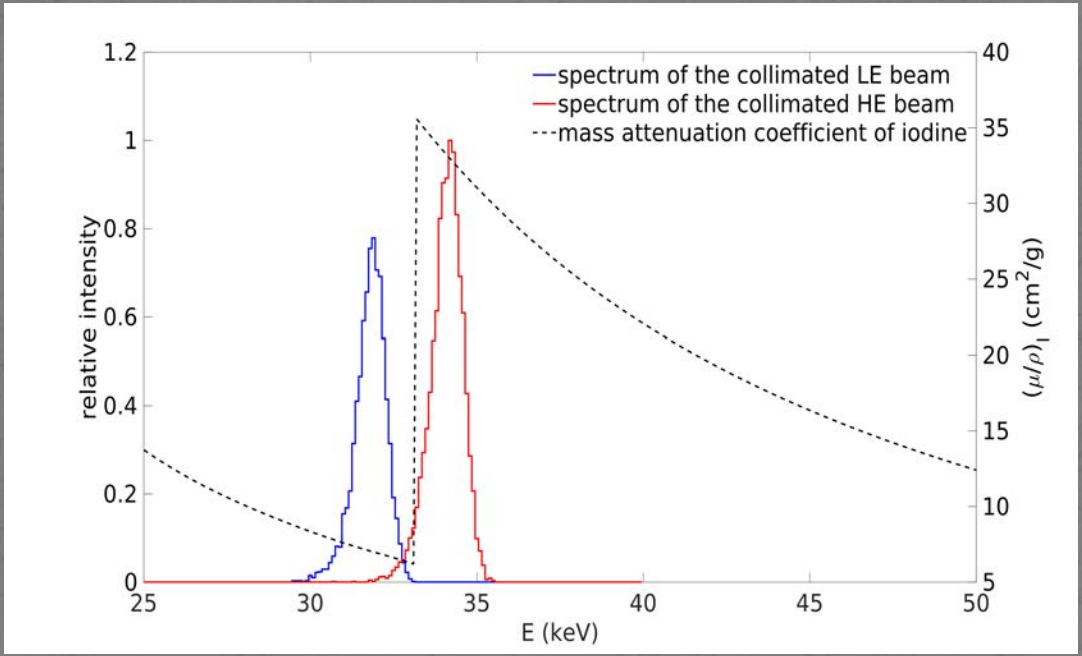




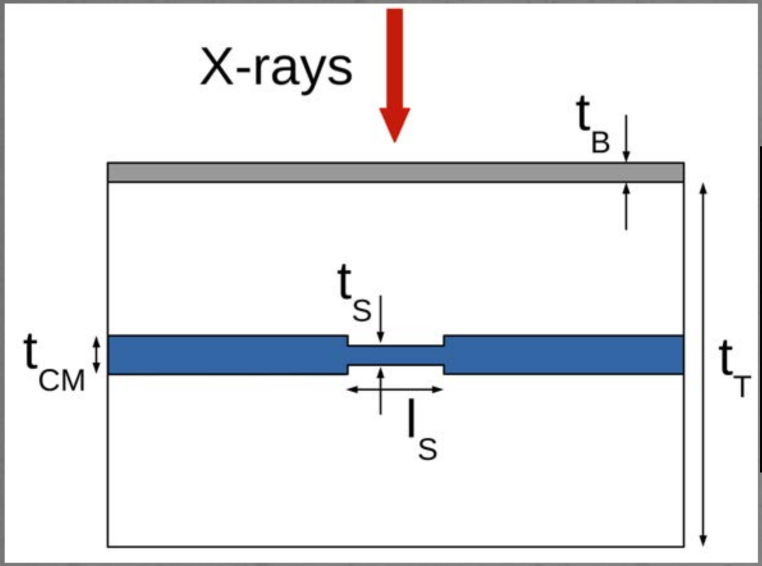
FABRY-PEROT CAVITY *(Drebot et al., IPAC2018,)*

It is possible to change the collision angle in a time of the order of 100 ms by switching the laser focus (tilting the curved mirrors) or the whole optical bench with two cavities.

Bracketing the Iodine k-edge …



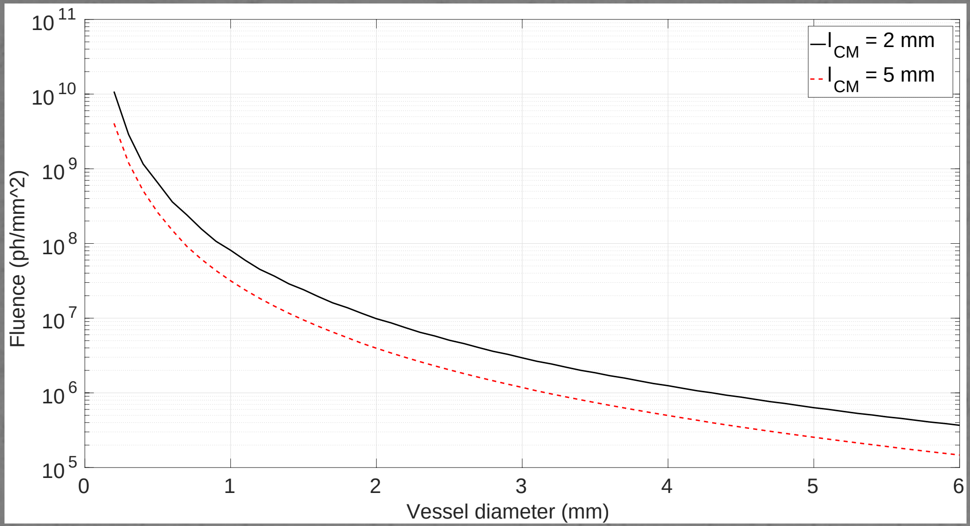
KES angiography with ICS sources

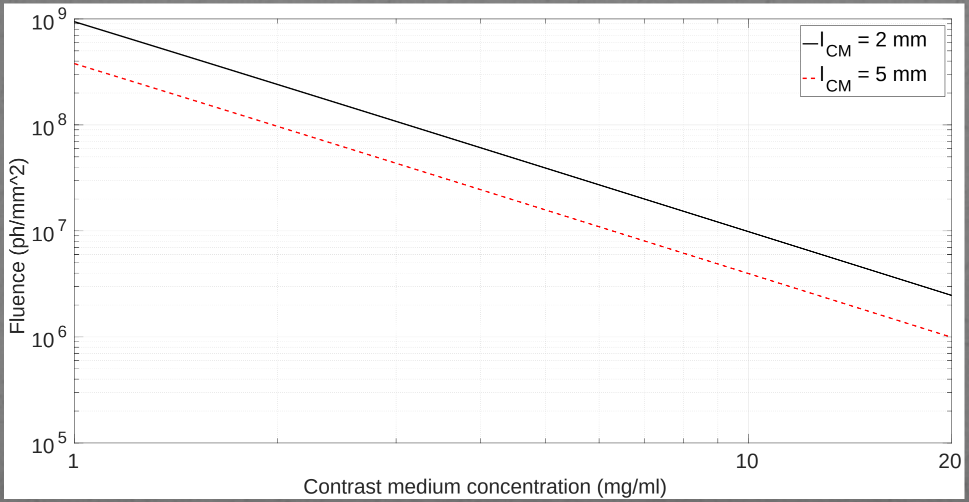


	t (cm)	μ^-/ρ (cm^2/g)	μ^+/ρ (cm^2/g)	ρ (g/cm^3)
Iodine	-	7.1100	33.5200	4.93
bone	1.0	0.8062	0.6888	1.41
Soft tissue	19.0	0.3501	0.3200	1.06

- Fluence required to obtain a SNR = 5 was estimated according to Sarnelli et al. Phys. Med. Biol. 51 (2006)
- Various vessel sizes and contrast medium concentrations were considered (within the range of clinical interest).
- The presence of the rib bone was also taken into account.

Results of the simulation

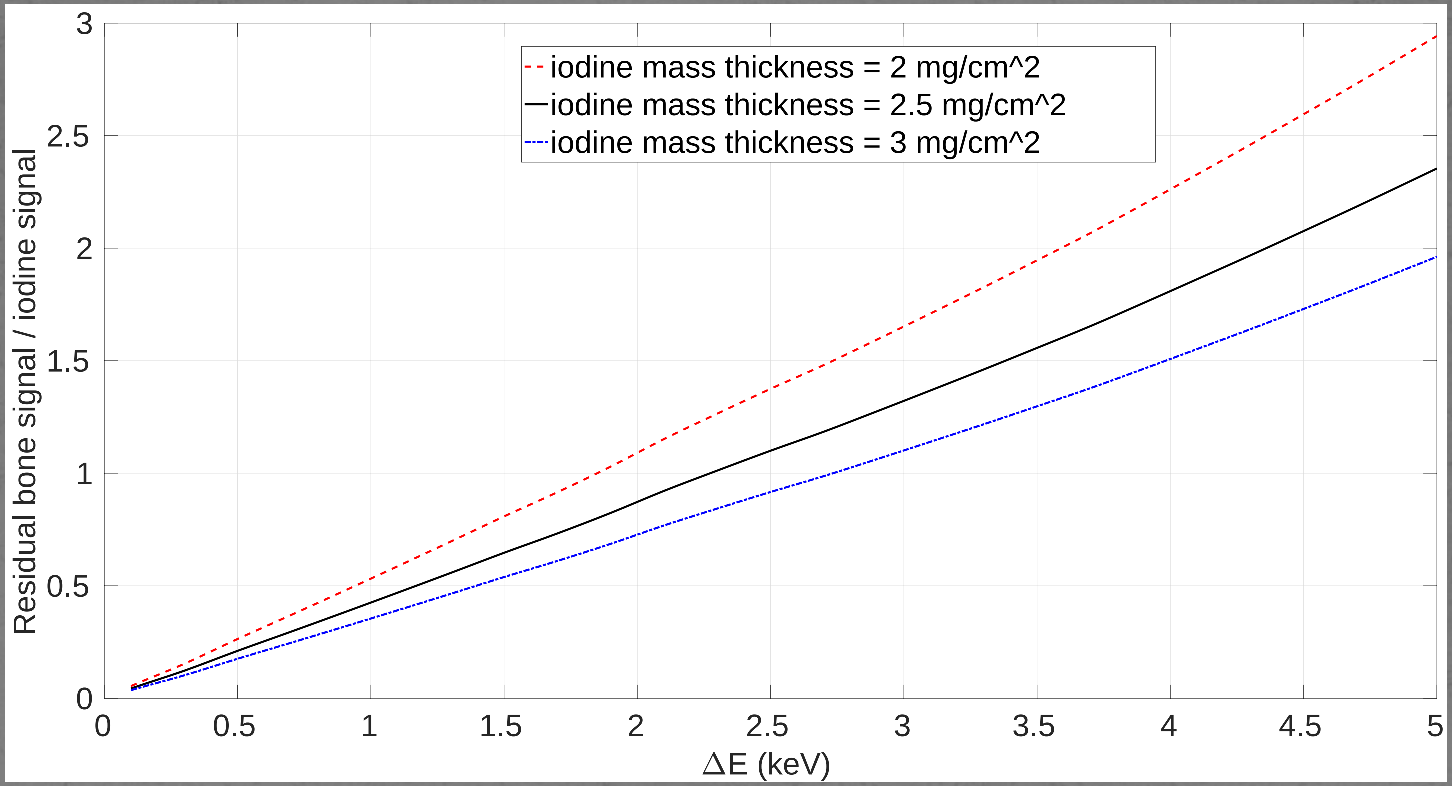




- SNR = 5
- c = 10 mg/ml

- SNR = 5
- Φ = 2 mm

Bone signal vs Energy separation



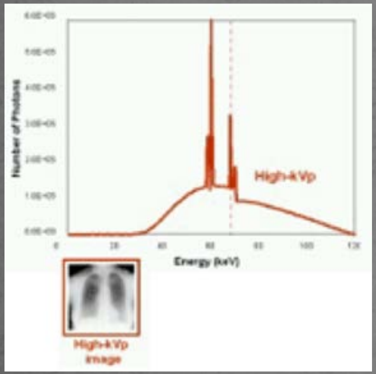
Current applications of Dual-energy

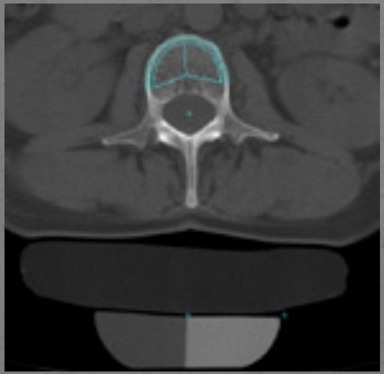
Without CA

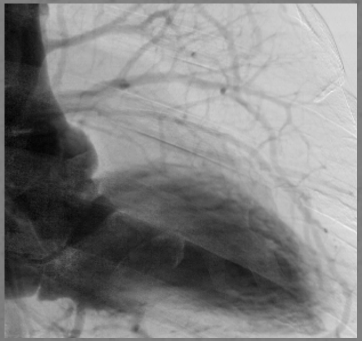
- Chest
- BMD (DEXA e QCT)

With CA

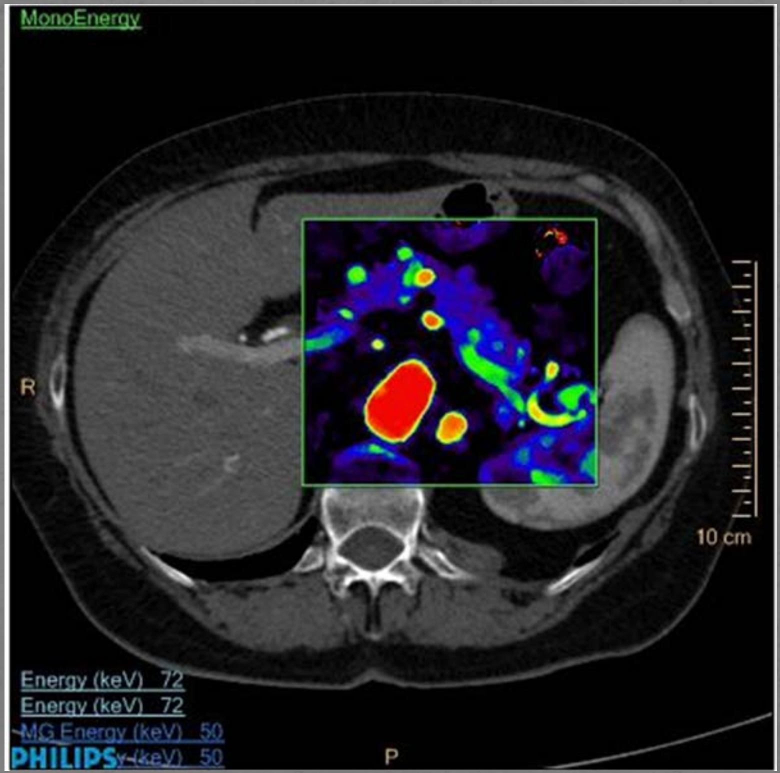
- CT
- DESA
- Mammog.





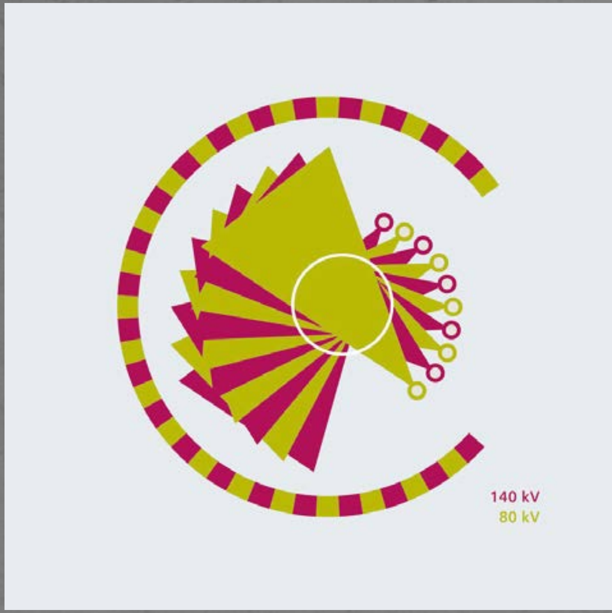


The future of X-ray imaging?

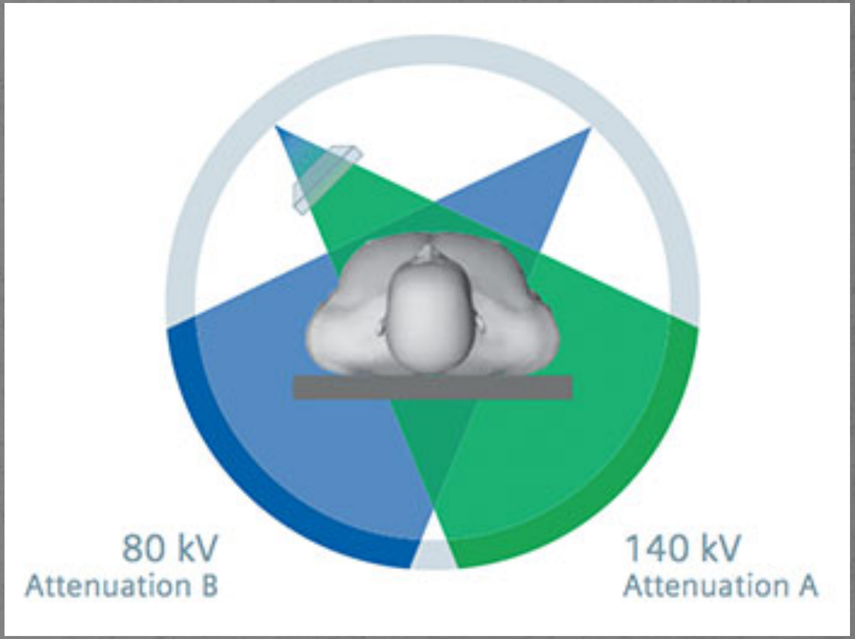


"X-ray attenuation is material specific and information about the object constituents can be extracted by spectral imaging"

Dual-Energy CT

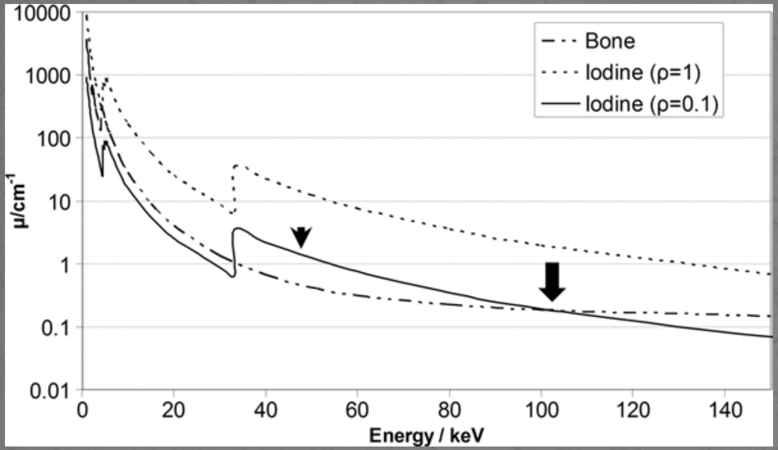


Fast kV switch



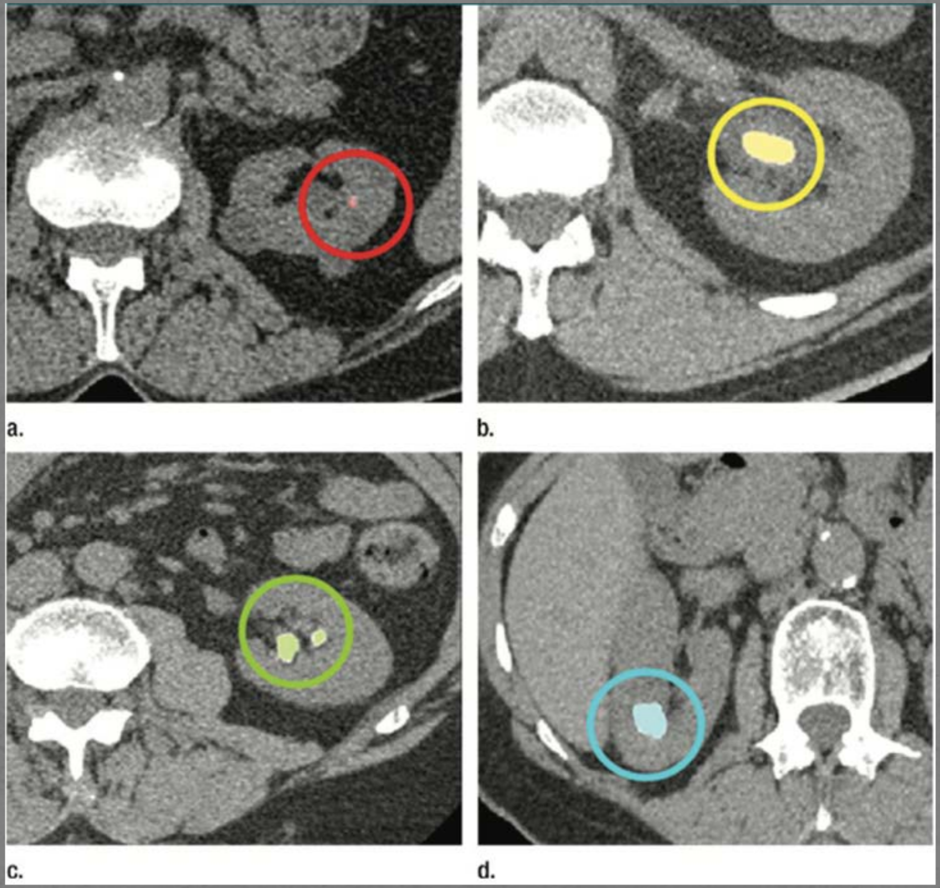
Dual X-ray source

Dual-Energy CT angiogram



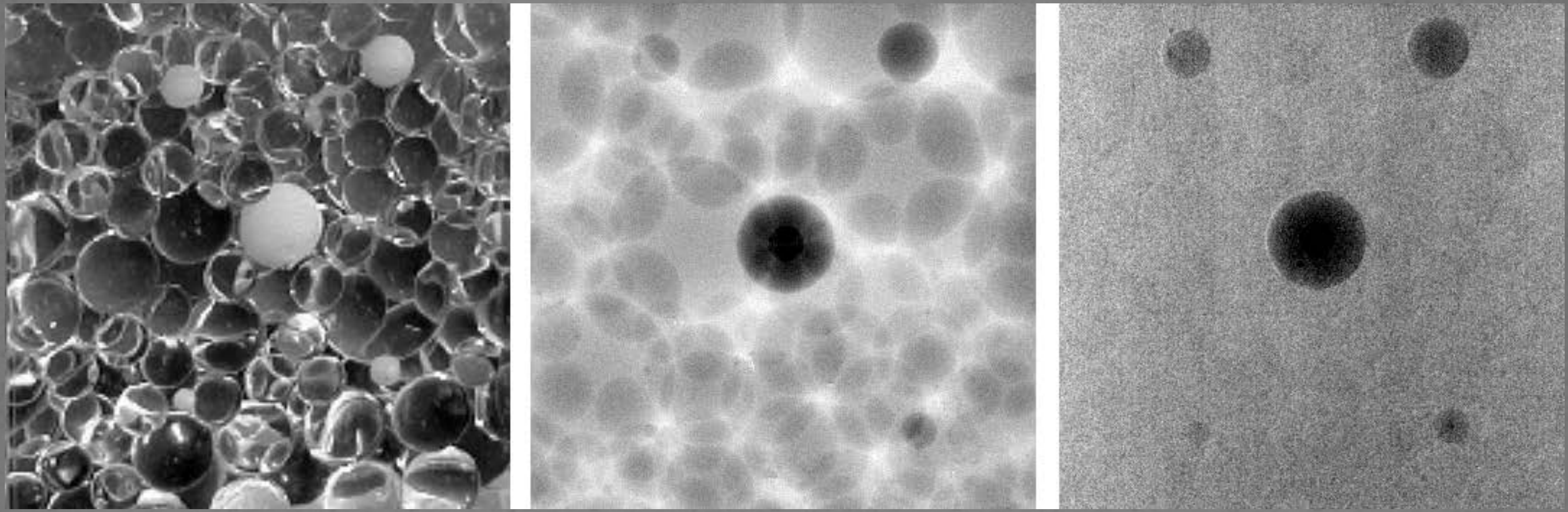
McCollough et al, Radiology 276, 2015

Potential benefits of SI: Tissue characterization



"The various types of non–uric acid stones contain higher Z elements and so distinguish themselves from the uric acid stones"

Potential benefits of SI: Background subtraction

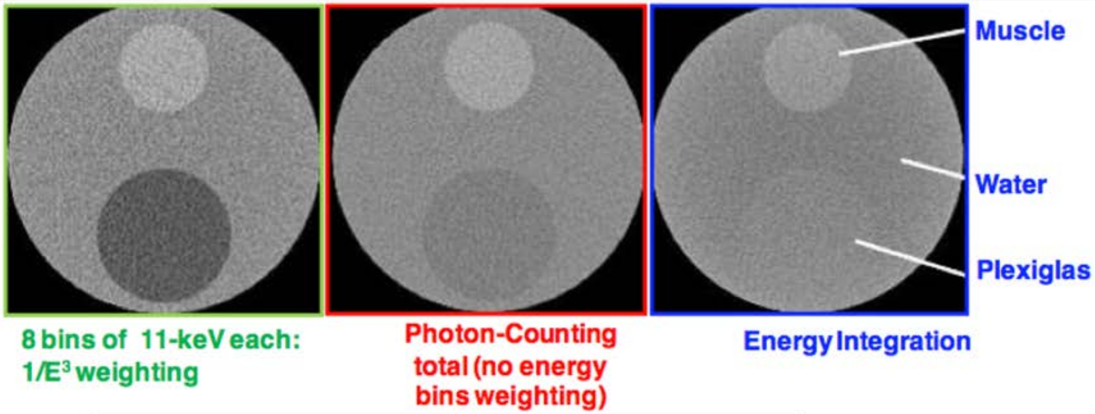


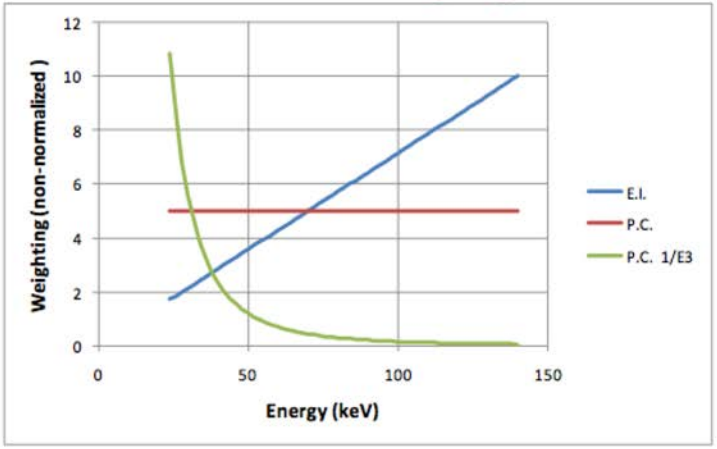
A Taibi *et al*, Phys Med Biol 48, 2003

"… from the clinical point of view, the complexity of anatomical structure … represents the ultimate limit to signal detection."

A Taibi, Eur J Radiol 72, 2009

Potential benefits of SI: Energy weighting

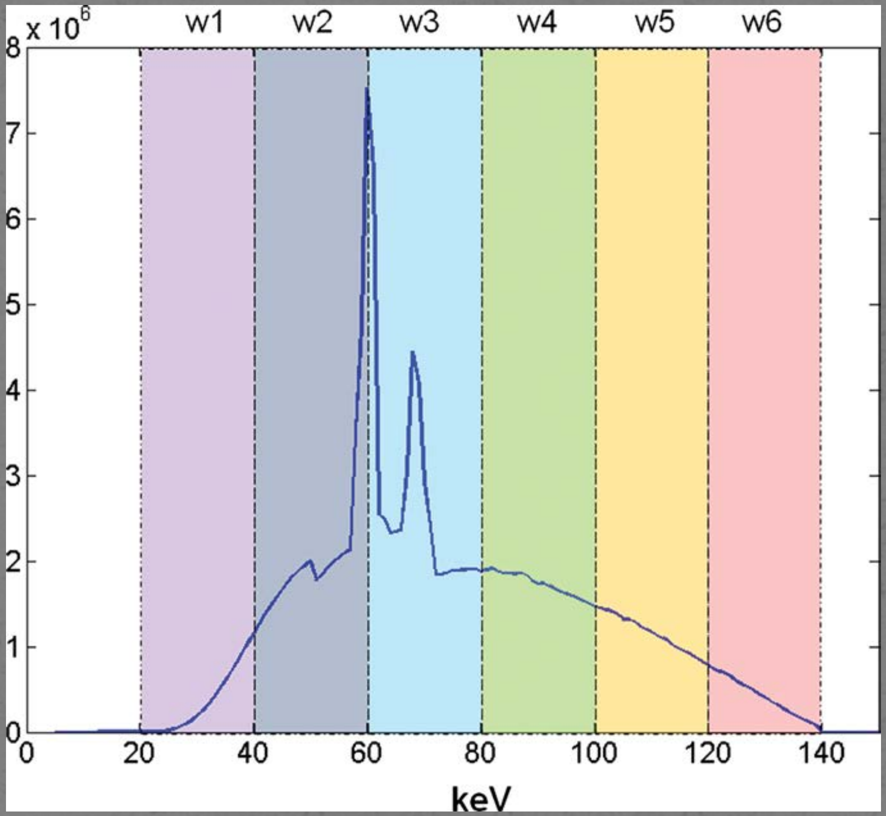




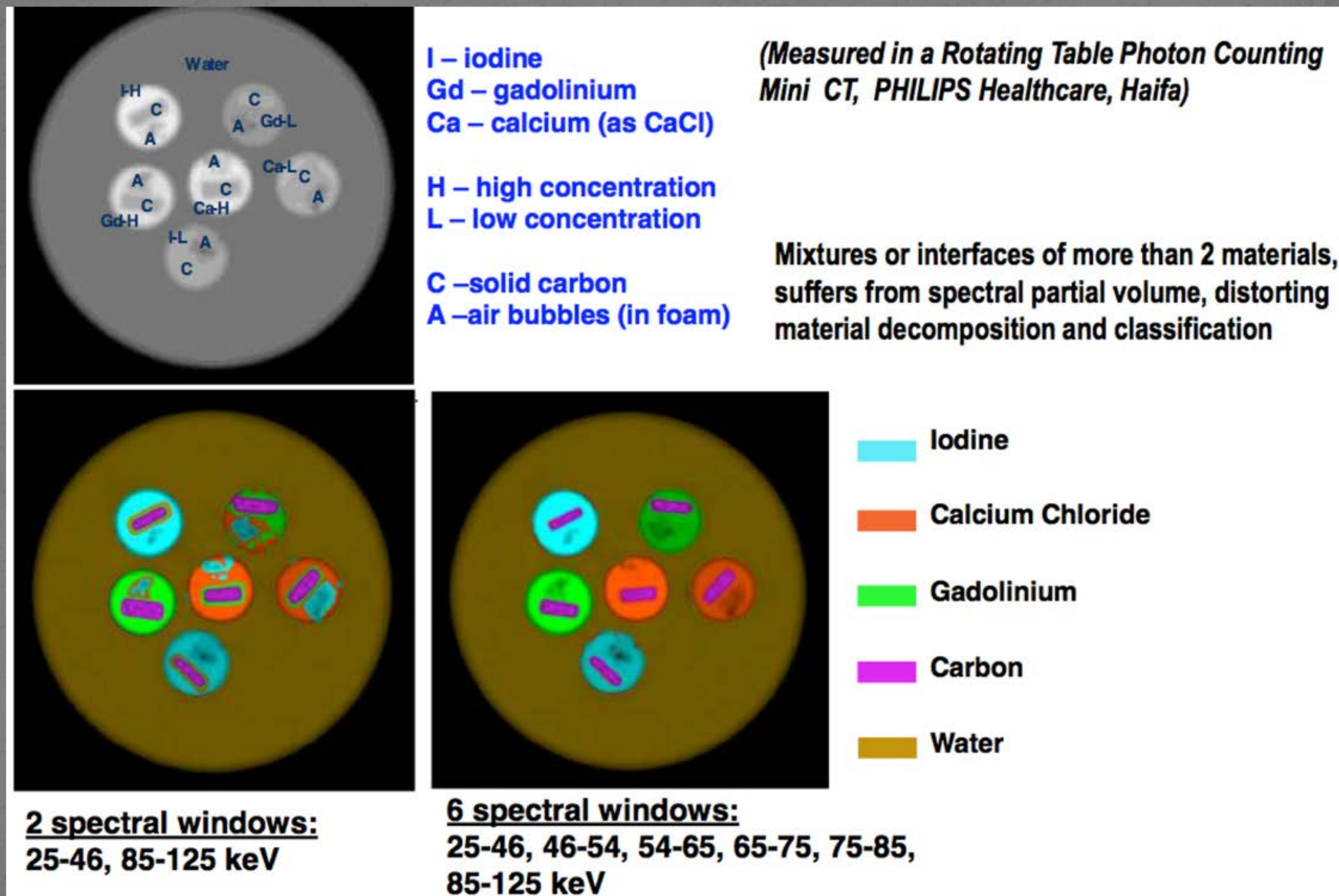
1. Z_eff of Plexiglas is ~20% < water
2. Energy Integrating over weights density over Z.
3. Photon Counting changes HU ratios, Contrast difference, and CNR
4. Opportunity to adapt energy weighting to specific applications
5. Potential increase in soft-tissue resolution.

"Reconstruction of the effective atomic number of materials"

Multi-Energy Imaging with PCD



Dual-Energy vs Multiple-Energy



Dual- and Multi-energy CT

Technology	Strengths	Weaknesses
Temporally sequential scanning of the entire scan volume	Can be performed on any CT scanner (no special hardware required).	Any patient motion occurring between the two scans may cause severe degradation of the resultant images and material composition information.
Temporally sequential scanning of a single axial rotation	Can be performed on any CT scanner (no special hardware required). Reduced interscan delay between the low- and high-energy images.	Best temporal resolution obtained with partial-scan reconstructions, which are more susceptible to errors in CT numbers; this might degrade material composition accuracy. The susceptibility to motion misregistration between the low- and high-energy single axial rotation may limit the value of this approach for imaging of vascular processes or tissues and organs susceptible to motion. For scanners having relatively narrow z-axis coverage, the increase in total scan time associated with an axial acquisition mode may be a limiting factor.
Rapid switching of the x-ray tube potential	Near-simultaneous data acquisition of the low- and high-energy data set. Allows dual-energy material-decomposition algorithms to be implemented by using either projection data or reconstructed images. Reduces beam-hardening artifacts in calculated "virtual monoenergetic" images.	Requires specialized hardware. Relatively high overlap of the energy spectra.
Multilayer detector	Simultaneous data acquisition of the low- and high-energy data set. All image data are acquired in a manner that supports material-specific imaging.	Requires specialized hardware. Relatively high overlap of the energy spectra. Noise level may differ between low- and high-energy images.
Dual x-ray sources	Tube current and tube filtration can be optimized for each tube potential independently. Relatively low degree of spectral overlap, which improves contrast-to-noise ratios in material-specific images. Beam-hardening corrections are applied prior to image reconstruction, allowing material-specific images to be created in the image domain.	Requires specialized hardware. A 90° phase shift between low- and high-energy data. Simultaneous use of both x-ray sources allows scattered radiation whose original primary photon came from one tube to be detected by the detector of the other tube, requiring specialized scatter correction.
Photon-counting detectors	Uses energy-specific measurements and energy thresholds to reject electronic noise. Facilitates new imaging approaches, such as k-edge subtraction.	Requires specialized hardware, which is not anticipated to be commercially available for some time, if at all.

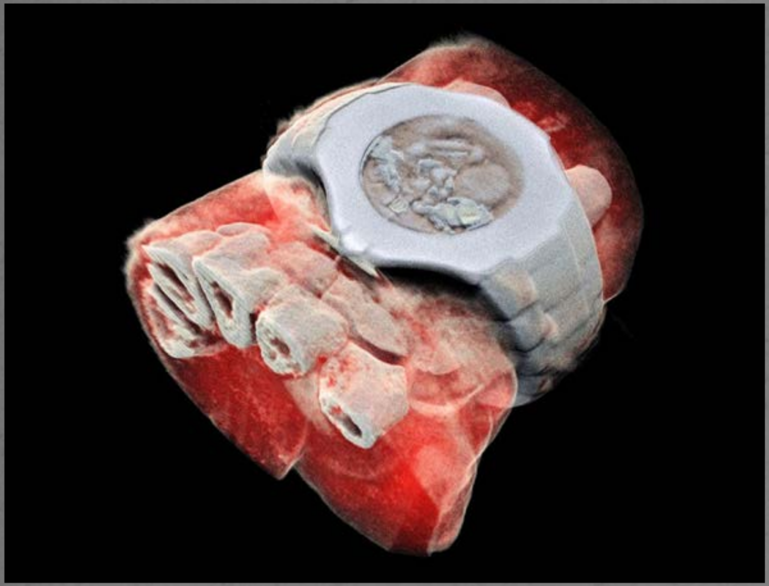
McCollough et al, Radiology 276, 2015

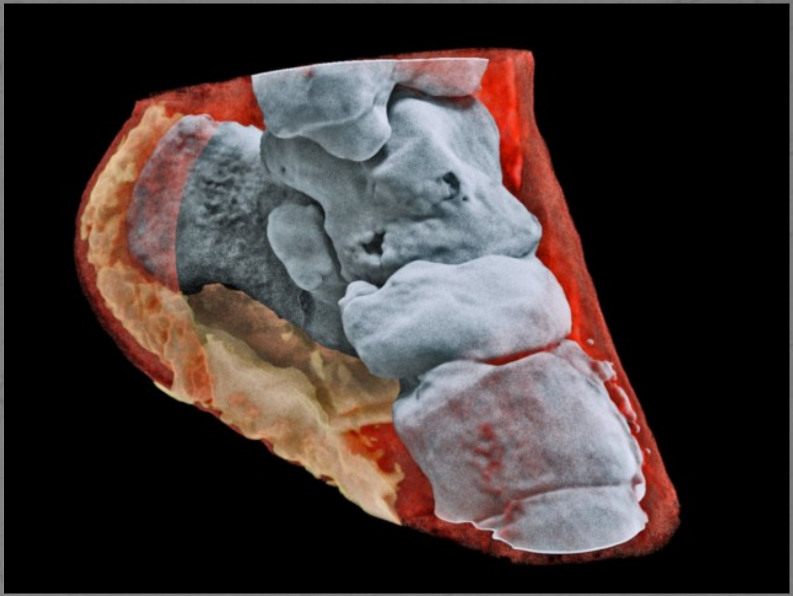
Comparison of PCDs

Index	Name/ASIC	Operation mode	Maximum count rates (Mcps/pixel)	Pixel size ($\mu m \times \mu m$)	Maximum count rates [Mcps/mm^2]	No. of energy thresholds per pixel	Tileup capability	Anti-charg sharing
1	DXMCT-1 (Refs. 5 and 8)		5.5	1000 × 1000	5.5	2	2D	No
2	DXMCT-2 (Ref. 20)		5.5[a]	500 × 500	22[a]	4	2D	No
3	Siemens 2010 (Refs. 17 and 28)		NA	225 × 225	NA	2 or 4[b]	NA[c]	No
4	ChromAIX (Ref. 16)		13.5[d]	300 × 300	150[d]	4	1D	No
5	Hamamatsu (Refs. 10 and 11)		1-2	1000 × 1000	1-2	5	1D	No
6	GMI CA3 (Refs. 6 and 9)		1-2	400 × 1000	2-5	6	1D	No
7	Medipix3RX (Refs. 13, 29, and 52)	FM[e]-SPM[f]	0.21[g]	55 × 55	69.4[g]	2	1D with 2 × N (3-side buttable)	No
		FM[e]-CSM[f]	0.036[g]	55 × 55	11.9[g]	1		Yes
		SM[e]-SPM[f]	0.145[h]	110 × 110	12[h]	8		No
		SM[e]-CSM[f]	0.034[h]	110 × 110	2.8[h]	4+4[i]		Yes
8	CIX (Ref. 15)		3.3	250 × 500	26	1	NA	No
9	Nexis Detector (Refs. 21 and 22)		2.0	1000 × 1000	2.0	5	1D	No
10	MicroDose SI (Silicon strip) (Refs. 24–26)		0.056[j]	50 × 50	NA	2	1D	Yes[k]
11	KTH Silicon strip (Refs. 23, 27, and 30–32)		2.5 or 7.5[l]	400 × 500	200 or 600[m]	8[n]	2D[o]	No

Taguchi and Iwanczyk, "Vision 20/20: Single photon counting x-ray detectors in medical imaging" Med. Phys. 40, 2013

3D colour x-ray images



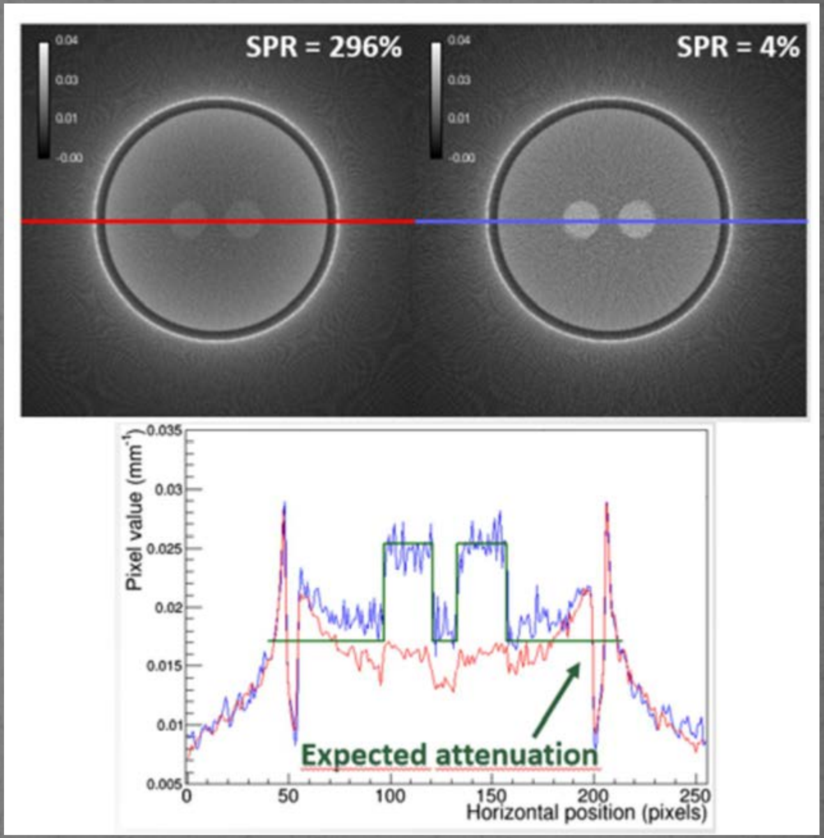


MARS Bioimaging Ltd

Time-of-Flight Imaging

- To get rid of scattered x-ray photons …
- A very short (and very intense) x-ray pulse is needed
- Detector has to be synchronized with the pulse …

Time resolution 10 ps!



Rossignol et al. J Nucl Med 2019

Small-animal imaging

"…To develop and validate non-invasive or minimally invasive imaging approaches to visualize pathological processes in pre-clinical mouse models."

- State-of-the-art services:
  - Magnetic Resonance (MRI)
  - Ultrasound (US)
  - Optical Imaging (OI)
  - Radioherapy (RT)
  - Computed Tomography (μCT)
  - Optical coherence tomography (OCT)

I.R.C.C.S. Ospedale
San Raffaele

- Concerning CT, very high DOSE is delivered …

Final Remarks

- YES, we are filling the gap but …
- We should focus on a specific application and optimize the x-ray beam characteristics (flux, field of view, energy, etc.)
- K-edge imaging is feasible but photon fluence is always a challenging parameter!
- Spectral imaging has a big potential:

  multi-energy x-ray source vs
  photon counting detector