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Review of medical imaging with emphasis on X-ray detectors

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Abstract

Medical imaging can be looked at from two different perspectives, the medical and the physical. The medical point of view is application-driven and involves finding the best way of tackling a medical problem through imaging, i.e. either to answer a diagnostic question, or to facilitate a therapy. For this purpose, industry offers a broad spectrum of radiographic, fluoroscopic, and angiographic equipment. The requirements depend on the medical problem: which organs have to be imaged, which details have to be made visible, how to deal with the problem of motion if any, and so forth. In radiography, for instance, large detector sizes of up to 43 cm × 43 cm and relatively high energies are needed to image a whole chest. In mammography, pixel sizes between 25 and 70 μm are favorable for good spatial resolution, which is essential for detecting microcalcifications. In cardiology, 30–60 images per second are required to follow the heart's motion. In computed tomography, marginal contrast differences down to one Hounsfield unit have to be resolved. In all cases, but especially in pediatrics, the required radiation dose must be kept as low as reasonably achievable. Moreover, three-dimensional(3D) reconstruction of image data allows much better orientation in the body, permitting a more accurate diagnosis, precise treatment planning, and image-guided therapy. Additional functional information from different modalities is very helpful, information such as perfusion, flow rate, diffusion, oxygen concentration, metabolism, and receptor affinity for specific molecules. To visualize, functional and anatomical information are fused into one combined image.

The physical point of view is technology-driven. A choice of different energies from the electromagnetic spectrum is available for imaging; not only X-rays in the range of 10–150 keV, but also γ rays, which are used in nuclear medicine, X-rays in the MeV range, which are used in portal imaging to monitor radiation therapy, visible and near infrared light (1–3 eV) for retina inspection and mamma transillumination, and even Terahertz waves (0.5–20 meV) are under discussion. Feasibility is determined by the existing radiation sources, the materials available for absorbing and converting the radiation used, the microelectronic circuits for integrating or counting readout, and the computing power required to process and, where applicable, reconstruct data in real-time. Furthermore, other physical effects can be utilized such as the phase information a wave front receives when passing through an object.

Some new developments will be discussed, e.g. energy-resolving methods for distinguishing different tissues in the patient, quanta-counting detection, phase contrast imaging, CCDs for very high spatial resolution, fast volume CT scanners, and organic semiconductors for a new generation of detection devices. Admittedly, apart from imaging performance, economic factors also have to be taken into account.

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1. Historical introduction [1]

The first X-ray image after the invention of this kind of electromagnetic rays by Prof. Wilhelm Conrad Röntgen in 1895 was taken from Prof. Röntgen's wife (Fig. 1a) on December 22, 1895. It was taken on a film, showing the finger bones and her ring. In the beginning of the 20th century, a scintillator screen was added to the film which resulted in quite an increase in sensitivity. Fig. 1b shows a radiologist's workplace with the patient who had to hold the film/screen cassette himself. But real-time imaging was

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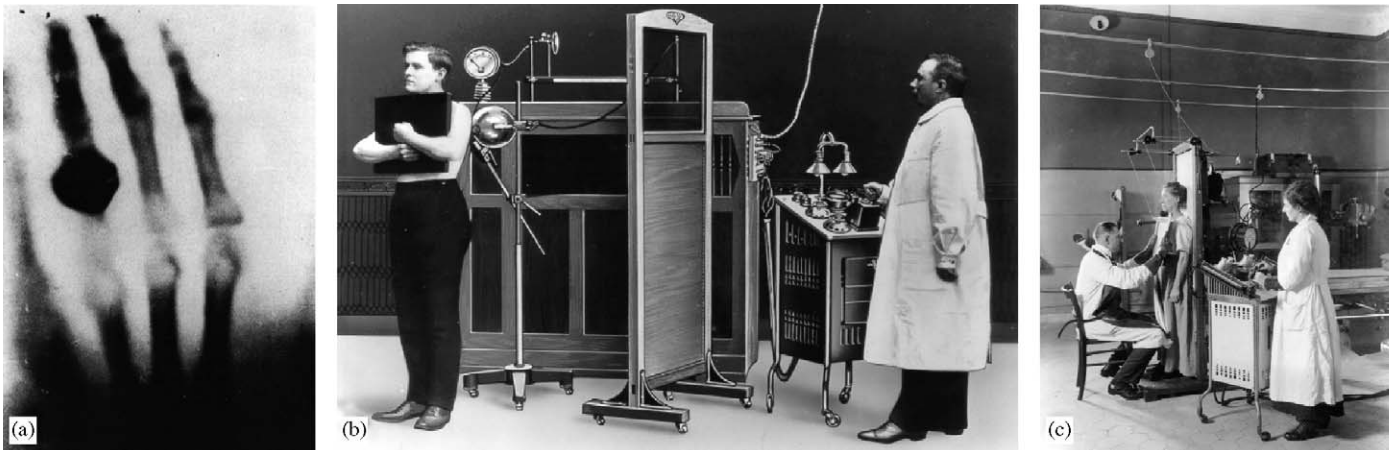

Fig. 1. (a) Ms. Röntgen's hand with ring (first X-ray image taken on December 22, 1895), (b) an early radiological workplace where the patient had to hold the film cassette himself, and (c) fluoroscopy in the Gynaecological Hospital, Erlangen (1918).

also feasible as can be seen from Fig. 1c showing an examination in front of a scintillating screen in the Gynecological Hospital, Erlangen, in 1918.

In the 1970s, analog fluoroscopy became widely used. This modality was realized by an X-ray image-intensifier tube coupled to a TV camera. Sometimes, this kind of system was also used to take single images where the image resolution, however, was limited by the camera performance. In the 1980s, X-ray radiography became digital by introducing the so-called computed radiography where a storage phosphor in a cassette is irradiated and later on read out by a laser scanner.

State-of-the-art all-digital X-ray imaging is accomplished by flat-panel detectors. [2] These detectors are based on a large-area semiconductor film, i.e. hydrogenated amorphous silicon (a-Si), forming an array of thin-film transistors (TFT) managing readout of the picture elements (pixels). The sensor in each pixel consists of a semiconductor layer, e.g. amorphous selenium, or an a-Si photodiode coupled to a scintillator film. An overview of imaging systems for medical diagnosis is given by Oppelt. [3].

2. Different points of view

Medical X-ray imaging can be looked at from different perspectives, from the medical and the physical point of view, respectively. The medical point of view is mainly driven by the application the physician aims at. Imaging is no longer limited for the purpose of medical diagnosis, but is becoming more and more important for image-guided interventions. Moreover, the images visualize not only simple anatomical features such as bones, tissue, and vessels, but increasingly, new imaging methods are applied to assess systemic functions such as perfusion, flow rates, diffusion, oxygen concentrations, metabolism, or the receptor affinity for specific molecules. Since morphology and function complement each other, image fusion where anatomical and functional information is combined to a joint image is advantageous.

The design of a medical imaging system has to take into account all the requirements which can be derived from analyzing the desired application. Many parameter requirements have to be fulfilled, e.g. detector size, speed, spatial and contrast resolution, but also workflow aspects have to be considered.

A significant improvement can be achieved by image processing and 3D reconstruction. A set of two-dimensional(2D) projection images taken from different angles can be used to reconstruct a three-dimensional(3D) data set. It can be used to calculate arbitrary cross-sections of the body, 3D views, or user-defined extracts by segmentation of the image data. These 3D images provide better orientation which is especially important for image-guided interventions.

The physical point of view, on the other hand, is technology-driven. Since imaging is performed in most cases by means of electromagnetic waves (magnetic resonance and ultrasound imaging will be ignored within the scope of this work), the key parameter is the wavelength to be used. Besides X-rays, imaging is accomplished by means of γ rays (in nuclear medicine), visible light (ocular fundus, skin), infrared light (mamma transillumination), or even Terahertz waves which has been proposed recently.

3. The medical point of view

In the following, a few examples will demonstrate the potential of medical imaging. A classical hand examination is shown in Fig. 2a, where a state-of-the-art radiographic system (Siemens AXIOM Artis FX®) is used. The X-ray tube is located at the top; the flat-panel detector can be seen on the bottom. The resulting hand image (Fig. 2b) depicts even fine details, but the full image quality, however, will only be available on a printout on a

Fig. 2. (a) Hand examination using a radiographic system (Siemens AXIOM Aristos FX®) comprising a flat-panel detector, (b) radiogram of a hand showing bones and nails, where soft tissue is barely visible, and (c) digital subtraction angiogram (DSA) of a hand with contrast media-filled vessels. The bones disappeared after subtraction of the native image, i.e. without contrast medium.

radiographic film or on a special monitor for radiographic images. Soft tissue yields little contrast and can thus be only barely seen in the image. In digital subtraction angiography (DSA) two images are recorded prior to and after administration of a contrast medium (in the majority of cases an iodine-containing solution) and then subtracted. Bones and tissues, which do not absorb contrast medium, will disappear; contrast medium-filled vessels will be displayed with high contrast (Fig. 2c).

A different example is breast examination for the diagnosis of cancer. The gold standard is the X-ray-based mammography, where a special radiographic unit is used. Its geometry allows for breast compression and oblique views and provides for a smooth workflow. Since the most critical objects in the breast tissue are microcalcifications some 100 μm in size which provide an indication for breast cancer, a high spatial resolution by the system is mandatory. Zooming of the final image visualizes and helps to detect small details. Computer-aided diagnosis (CAD) is suitable for providing a second opinion, helping the radiologist not to overlook a suspicious item. This increases the sensitivity of the diagnosis. Since there are plenty of different benign and malignant breast lesions which are very difficult to identify, the investigation must be conducted by a radiologist with many years of experience. If there is any remaining doubt, complementary methods such as ultrasound (US), magnetic resonance imaging (MRI), or optical tomography can be helpful.

In the case of cardiac disorders, different medical imaging procedures can be deployed. A non-invasive method which delivers 4D information is an electrocardiogram (ECG) —gated computed tomography angiography (CTA) scan. The ECG allows a series of images taken in the same phase of the heart beat to be combined and reconstructed. An US examination can reveal extra information. A combined diagnostic and treatment procedure is percutaneous transluminal coronary angioplasty (PTCA). A catheter is introduced through the iliac artery up to the heart and an iodine-based contrast agent is admitted. This enables the visualization of the coronary arteries and the diagnosis of, e.g. coronary plaques or a stenosis. The same procedure then allows the clogged artery to be widened by inserting a balloon and inflating it with high pressure (balloon dilatation). Placing a stent assures against the risk of a restenosis. The whole PTCA is carried out under fluoroscopy control.

A totally different kind of medical imaging should also be mentioned, optical imaging of the ocular fundus. Optical imaging of the retina is the only way to examine veins directly and non-invasively. This very easy assessment allows the risk prediction of vascular diseases, e.g. stroke or diabetes. [4] The data can also be simply transmitted to remote places for diagnosis by experts who are not available on-site. Tele-ophthalmology has been demonstrated in a large international project.

Another optical imaging method is Optical Coherence Tomography (OCT) for the examination of vessels. The inner wall of a vessel is illuminated by a broadband source via a catheter and a rotating mirror. The reflected light is analyzed and provides an image of the vessel which reveals details of the lesion pathology. This allows the visualization of vulnerable coronary plaques, calcifications, or the correct stent placement to be checked.

The medical X-ray imaging methods can be divided up into two different classes, full-field and scanning imaging. Simple full-field projection imaging uses an X-ray tube; the emitted radiation penetrates the patient to be examined and is registered by the detector. The required detector size is given by the patient region of interest times the magnification factor of the projection geometry. The

X-ray exposure time of the detector is equal to the duration of the X-ray emission of the tube. This full-field technique is used in the majority of cases.

The alternative approach is scanning imaging. In the ideal case, a very narrow slit in front of the X-ray tube selects a fan beam which is scanned across the patient and absorbed in a one-pixel-wide line detector. This idealized concept is not feasible because the fraction of radiation passing the collimator is too low. A slot detector that is several pixels wide requires time-delay and integration (TDI) technique and a collimator restricting the beam to the detector width. Due to the extended focus size a penumbra region around the detector occurs. This leads to radiation loss and thus to an increased patient dose. All scanning systems require a precise mechanical setup to assure accurate synchronization of collimator and detector movement. The whole scan takes about 5 – 20 s in most systems on the market, which might cause motion artifacts. Since the X-ray tube has to emit radiation throughout the whole scanning cycle, the tube load will become very high and may cause problems. Current X-ray tubes often operate close to their technological, i.e. thermal limits. Therefore, full-field imaging is superior to scanning imaging in most cases.

The different medical applications allow for the derivation of requirement specifications for the fundamental detector parameters. [5] The detector size, for instance, must fit the region of interest (ROI) which is given by the human body. Therefore, the largest X-ray detectors used in radiology have an active area of 43 cm × 43 cm which is necessary to image chest or pelvis. Detectors for the whole range of applications such as fluoroscopy, angiography, or neurology are somewhat smaller, e.g. 30 cm × 40 cm.In mammography, typical formats are 18 cm × 24 cm or 24 cm × 30 cm for small and large breasts, respectively. Cardiology can manage with relatively small (20 cm × 20 cm) detectors which allow extreme angulations and are favorable for ergonomic reasons. Apart from dental imaging, smaller detectors are only applied in mammography biopsy, where formats of 5 cm × 9 cm are sufficient. This can be realized with large CCDs. A different situation is given in computed tomography where the whole width of the body has to be imaged. State-of-the-art CT systems use curved multi-slice detectors with a total size of some 4 cm × 70 cm.

Since CT gantries rotate very fast around the patient, between 2000 and 6000 images per second are taken. The frame rates in fluoroscopy and cardiology are 15–60 s^{-1}, while in angiography (DSA) 2–30 s^{-1} are required. In ordinary radiography and mammography only single images are taken. Since the patient has to be repositioned between two exposures, a rate of one image every 20 s is sufficient in majority of cases.

The pixel size and the required spatial resolution depend on the objects to be imaged. For soft tissue and vessels some 1–2 mm^{-1} have to be resolved which requires a pixel size of 150–400 μm. Bones with fine fissures and a trabecular structure need 3–4 mm^{-1}. The respective detectors have pixels as small as 125–165 μm. In mammography and dental imaging the smallest details of interest occur, e.g. microcalcifications which are some 100 μm in size. The system should therefore resolve 5–20 mm^{-1}. The detectors on the market have pixel sizes of 100 μm or less.

4. The physical point of view

Under a very general perspective, imaging needs a radiation source, an interaction with the object to be imaged, an ensuing registration of the radiation bearing information about the object, and possibly image processing. The radiation source can be a monochromatic source or, as in most practical cases, an X-ray tube emitting a broad spectrum. The latter is modified by applying absorption filters resulting in a spectrum with a more or less broad spectral range. Moreover, the spatial extent of the source is crucial for the imaging properties. The coherence might be of interest in the case of phase-sensitive imaging.

The fundamental interaction of electromagnetic radiation with matter is absorption which is energy dependent. Beyond that, reflection, scattering, diffraction, and refraction may occur. The whole succession of processes can be studied, e.g. by Monte-Carlo simulations. [6] Details of interest should differ in their interaction behavior compared to the surrounding tissue. This will result in a contrast whose magnitude compared to the ubiquitous image noise determines its visibility.

Registration of the radiation behind the object which bears the information of interest requires a detector. The interaction in the detector will be again in most cases absorption, either by a directly converting semiconductor or by a scintillator followed by a light sensor, e.g. a photodiode. In this way radiation is converted into an electrical signal. The sensitive area of a detector is divided up into an array of detector elements. Each element delivers a signal representing the amount of radiation absorbed therein. The signal can be used in two different ways. Either the signal is integrated over a certain time which is called integrating detection, or every single event is analyzed individually which is called counting detection. The latter case opens up the opportunity of discriminating between individual quanta according to their energy or potentially a temporal correlation to other events (coincidence detection in positron emission tomography).

X-ray imaging as an example shall be discussed in detail. It is evident that an X-ray spectrum with rather low energies will be absorbed strongly in the body under examination hence leading to little signal at the detector. On the other hand, high-energy quanta are scarcely absorbed but also lead only to poor contrast. Somewhere in-between an optimum energy can be found with the maximum signal at the detector. This optimum energy strongly depends on the object to be imaged. Typical energy ranges e.g. for mammography are 17–25 keV, for radiography 40–60 keV, for computed tomography 60–70 keV, and for angiography around 33 keV, which is the K-edge energy of iodine used as a contrast medium.

A monochromatic radiation at the respective optimal energy would be ideal, but is in general difficult to produce. Therefore, polychromatic spectra are used with an average energy close to that ideal energy. This can be accomplished by an appropriate choice of anode material, tube voltage, and beam filtration (i.e. filter material and thickness).

Of course, many additional factors influence the quality of the resulting images. The non-zero focus size of the source leads to image blurring and thus to a reduced spatial resolution. Scattered radiation is especially important behind thick objects and overlays the image content, reducing the contrast of the details of interest and adding quantum noise. A proven remedy is an anti-scatter grid. Needless to say, the fundamental detector properties, e.g. modulation transfer function (MTF), detective quantum efficiency (DQE), or image lag strongly determine the quality of the resulting image. Nevertheless, this will not be discussed here.

The commonly used X-ray source is a tube with a W anode, which is favorable because it can withstand high temperatures. The emission line $K\alpha$ of W is 59.3 keV, so that mainly the X-ray continuum is used. Mo and Rh anodes are also used, since their dominating emission lines ($K\alpha$) of 17.5 and 20.2 keV, respectively, are especially suitable for mammography applications. Additional filters such as Al, Cu, Mo, or Rh are used to cut off the low-energy part of the spectrum, which results in a considerable dose reduction for the patient.

The detectors that meanwhile have penetrated the market are flat-panel solid-state detectors (FD) based on a read-out matrix of amorphous silicon (a-Si) thin-film transistors (TFT). The X-ray absorption layer can be an amorphous Se layer which directly converts X-ray quanta to charge carriers which subsequently become stored and read out. This technology is favorable for mammography because it combines very good spatial resolution with high absorption. [7] At higher energies, i.e. for radiography, fluoroscopy, and angiography, the indirect detection concept is applied. A scintillator converts incoming X-ray quanta into visible light which in turn is registered by an array of amorphous silicon photodiodes. In the majority of cases the scintillator is evaporated cesium iodide which features a columnar structure with an inhomogeneous light propagation. Therefore, an adequate spatial resolution can be maintained even at scintillator layers as thick as 600 μm. In computed tomography, the energies are higher, the absorption should be above 90%, and the transient response must be in the order of μs, whereas for the moderate spatial resolution required a pixel size of 0.5–1 mm is sufficient. Here a combination of a fast ceramic scintillator (Gd_2O_2S) with c-Si photodiodes is beneficial.

Additional means are mandatory for good imaging properties. An anti-scatter grid which suppresses radiation from directions deviating from the direct connecting line between X-ray source and detector element is necessary in most cases to suppress scattered radiation and thus improving the contrast of the details of interest. In CT, collimators are indispensable since scattered quanta would deteriorate the 3D reconstruction calculations. The analog detector output signals are converted to digital, whereas the analog-to-digital converter requires a resolution of 12–16 bit for FD and 18–20 bit for CT. A sophisticated signal processing is also necessary including offset subtraction, gain correction for each individual pixel, interpolation of missing information from dead pixels, and compensation of correlated noise. Furthermore, methods such as edge enhancement, temporal filtering, gray scale look-up tables, and auto-windowing are applied to deliver perfect-looking images.

Finally, nuclear medicine should be briefly mentioned as a complementary principle for medical imaging with ionizing radiation. In this case no external radiation is used to scan the object. In fact the source distribution inside the patient has to be determined. A tracer with radioactive isotopes is injected or administrated orally. Then the tracer distributes in the body and accumulates in the region of interest, e.g. a tumor. The emitted radiation is mapped by means of a collimator (Single Photon Emission Computed Tomography = SPECT) or in coincidence using two detectors (Positron Emission Tomography = PET). Subsequently, 2D or 3D iterative reconstruction, filtered back projection, and attenuation corrections are performed. The detectors can be scintillators (e.g. BaF_2, $Bi_4Ge_3O_{12}$ = BGO, Lu_2SiO_5 = LSO, NaI) coupled to photomultiplier tubes or semiconductor detectors such as CdZnTe (CZT).

5. New concepts

In recent years, several advanced imaging solutions have been realized or currently are under development. In the following, some of these technologies will be presented.

5.1. *CCD-based detectors for very high spatial resolution*

As mentioned above, FD detectors are suitable for most X-ray imaging applications. They are based on an a-Si readout matrix, each pixel comprising an a-Si switch and a sensing element. The restricted space available leads to a minimum pixel pitch of some 70 μm, otherwise the spatial fill factor of the pixels would become too low. Especially for mammographic biopsies imaging with very high resolution is desirable. Therefore, a CCD-based detector has been developed with a pixel pitch of 12 μm. It can be also used in a 2×2 or 4×4 binned mode, resulting in 24 or 48 μm pixels, respectively. The detector uses a CsI scintillator which is coupled via a fiberoptic plate to the sensor with 4 K $\times$ 7 K pixels. The sensitive area is 49 mm $\times$ 86 mm being the largest CCD in serial production in the world [8] (see Fig. 3).

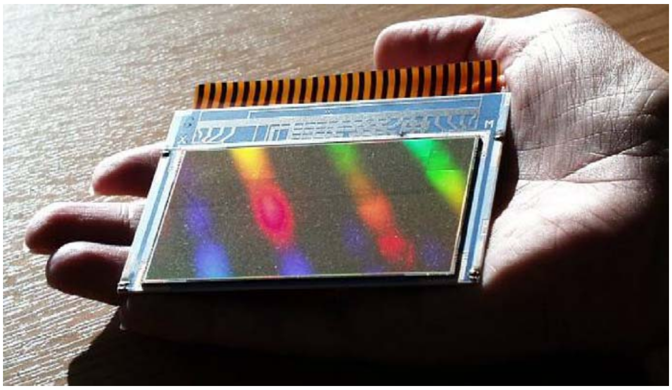

Fig. 3. The CCD of the OPDIMA sensor with a 7 K × 4 K matrix is 86 mm × 49 mm in size.

5.2. Organic semiconductor-based detectors

Current FD detectors are based on a-Si technology that has proven to be suitable for radiological, fluoroscopic, and angiographic applications. These detectors are built on glass substrates which are rigid, heavy, and fragile. The a-Si layers and electrodes are patterned by photolithography, a process enabling the production of fine structures. Depositing a-Si requires elevated temperatures in the order of 250 °C. In summary, there is also a demand for cheaper alternatives to a-Si technology.

Some investigations are going on into all-organic detectors. [9] Plastic substrates can be used which are flexible, light-weight, and unbreakable. The organic semiconductor and electrode layers can be deposited in the desired pattern, e.g. by jet printing. This results in cheap detectors which have the potential for new applications. Since an organic detector is not as heavy as an a-Si-based detector, it lends itself to use in a portable bed-side device. It has been shown that organic photodiodes and transistors are feasible, but further work is necessary to improve their performance.

5.3. Fast volume CT scanners

Today's computed tomography scanners show outstanding features for X-ray imaging diagnostics. The data acquisition rate is so high that a whole body scan can be completed within 25 s. Moreover, it is feasible to reconstruct a beating heart. The bases for this outstanding performance are technologies that have been pushed to their limits. The gantry with X-ray tube, generator, cooling unit, and detector has a rotation time as short as 0.33 s. The multi-slice detector used records 64 slices per revolution. It utilizes a fast ceramic scintillator (Gd_2O_2S) together with silicon photodiodes. The scintillator allows the absorption of >90% of the incident radiation which results in an outstanding DQE. In addition the response is extremely fast which is essential for the quickly rotating gantry.

A technological highlight is the Siemens Straton® X-ray tube. Conventional tubes suffer from the fact that they are thermally limited in their power output due to the slow heat exchange from the anode, rotating in a vacuum, to the cooling oil. In the Straton® tube the whole tube rotates with the anode integrated in the tube wall and thus in direct contact with the cooling oil. This allows an extremely high permanent load which is necessary to perform numerous examinations in fast sequence.

5.4. Energy-resolving methods

All conventional medical X-ray imaging methods, e.g. film, storage phosphor, image intensifier, FD scintillator + photodiode, FD directly absorbing, CT, are based on X-ray absorption. Thus they image the total absorption of an object. Admittedly, different combinations of matter in a body can produce equal total absorption. Since the energy dependence of X-ray absorption is different for each chemical element, equal absorption at one energy will lead to a different absorption at a higher or lower energy. Therefore, energy-resolving methods (ERM) can differentiate between different objects.

The goal of ERM is to improve the detectability of details and enhance their signal-difference-to-noise ratio (SDNR). This not only allows discrimination between different materials or kinds of tissue, but also the enhancement of the visibility of contrast media. In the end, ERM allows for dose reduction, while maintaining SDNR and thus image quality. Moreover, contrast media can be saved which reduces patient stress and costs.

ERM is applied in the non-medical field, e.g. for security flight baggage inspection where it is necessary to discriminate explosives from other belongings. In medical diagnosis, ERM is widely used in bone mineral density measurements by Dual-Energy X-ray Absorptiometry (DEXA) or Dual-Photon Absorptiometry (DPA) where it is necessary to quantitatively investigate the bones independently of the surrounding soft tissue.

In chest examinations ERM is applied by exposing the patient twice with different X-ray spectra, i.e. different tube voltage settings and different prefiltration. Fig. 4 shows two chest images taken with a low and a high energy spectrum. A weighted difference image makes ribs and spine disappear and offers an undisturbed view on the lung tissue. This is especially useful for finding low-contrast nodules as an indication for lung cancer. Changing the parameters can lead to a bone image. Sophisticated algorithms are applied to reduce the noise in the images, as has been discussed by Avinash et al. [10].

Dual-energy contrast-enhanced digital subtraction mammography has been introduced by Lewin et al. [11] . Fig. 5 shows a series of mammograms taken with different spectra and prior (3A)/after contrast medium admission. The images 3B and 3C are taken with low and high energy, respectively. The subtraction image of 3C and 3B, 3D,

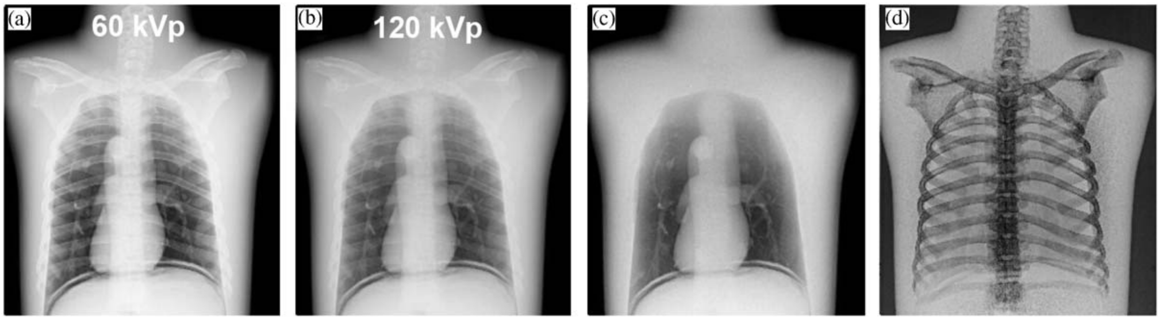

Fig. 4. Two chest radiograms taken with a low (a) and a high (b) energy spectrum. Applying an appropriate algorithm can make ribs and spine disappear and offer an undisturbed view on the lung tissue (c). Different weighting (d) leads to a bone image (from Ref. [10]).

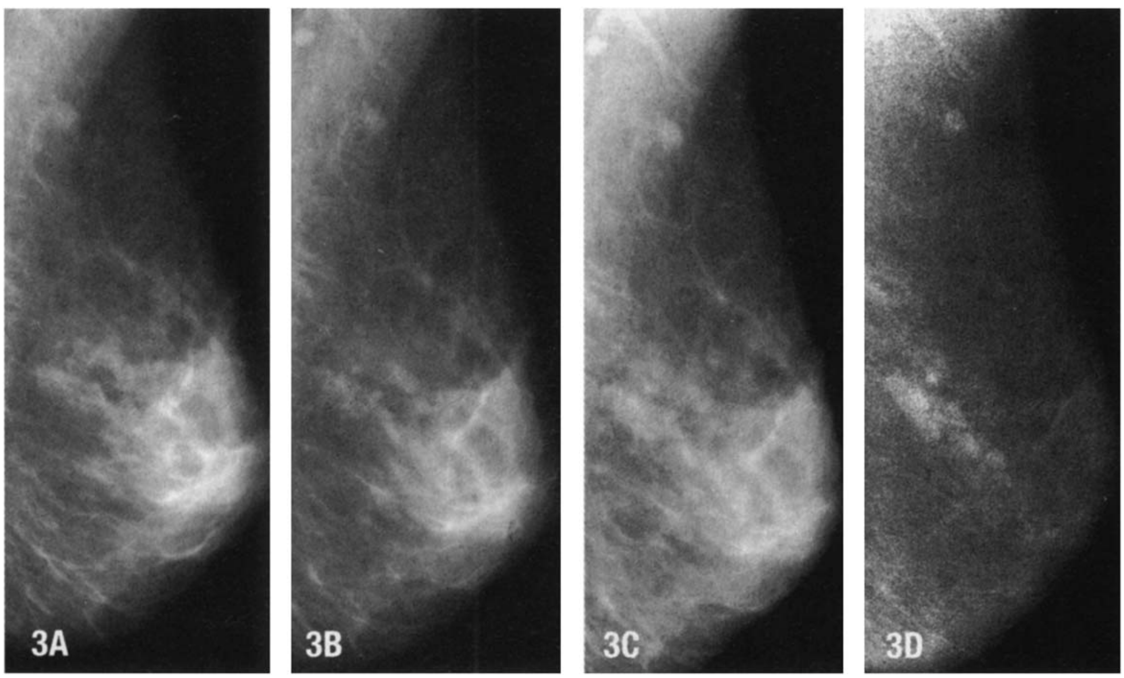

Fig. 5. Nonpalpable invasive ductal carcinoma and ductal carcinoma in situ (DCIS). 3A: Precontrast digital mammogram shows calcifications of DCIS. 3B: Post-contrast low-energy mammogram. 3C: Post-contrast high-energy mammogram. 3D: Dual-energy contrast-enhanced digital subtraction mammogram. Enhancing masses corresponding to the invasive cancer are easily visible after subtraction, but are not readily appreciated on the unsubtracted images, 3B and 3C (from Ref. [11]).

shows an invasive cancer which could not be detected in the single images 3B and 3C.

5.5. *Quanta-counting detection*

Whereas in conventional X-ray imaging an energy-integrated signal is used, single quantum counting offers several advantages. In principle a higher DQE should be obtainable because every quantum produces an equal count irrespectively of its energy. Moreover, a counting detector operates independent of electronic noise. Once the discrimination level for detection is fairly above the noise floor only desired quanta will be registered and can be counted. The detector already delivers a digital signal and no analog-to-digital conversion is necessary. Perhaps the most interesting feature is the possibility of distinguishing between quanta of different energy. This allows gaining much more information from a radiation field compared to the summary signal delivered by an integrating detector. Several discriminators have to be implemented to define energy intervals. Events in each energy interval will be counted separately.

Admittedly there are also disadvantages for quanta counting. Amplifier, discriminators and counters have to be small enough to fit in the pixel area. When the detector is exposed to higher dose levels, the count rates especially at larger pixels can be very high (some $10^6 - 10^7\,s^{-1}$) which necessitates a very fast readout electronics to avoid pile-up effects. Therefore, especially for higher doses, integrating detectors are the simpler and cheaper solution.

First investigations towards the application of a counting detector for medical applications have been carried out with the Medipix-2 chip coupled to a semiconductor absorber. [12] The Medipix-2 chip comprises 256×256 pixels $55\,\mu m \times 55\,\mu m$ in size. Of course its overall size of $14\,mm \times 14\,mm$ is too small for medical applications, but it can be tiled for instance to form a 2×4 chip array on a chip board. Different semiconductors slabs, preferably with a high atomic numbers Z, as absorbers for good DQE, can be bump-bonded to the Medipix-2 chip, e.g. Si, GaAs, CdZnTe, CdTe. But also HgI_2, InSb, TlBr, or PbI are under discussion.

5.6. Monochromatic X-ray imaging

The advantages of monochromatic X-ray imaging have already been discussed above (see Section 4). To evaluate the advantages in the case of medical applications in detail, an experimental setup is necessary. All methods using a synchrotron have been ruled out since it is too expensive and not a smart device we favor for medical diagnosis. A feasible solution we investigated is a bent Highly Oriented Pyrolythic Graphite (HOPG) crystal as a monochromator which directs the radiation onto a slot in a collimator. The detector used was a TDI-CCD Thales TH9570; the scan time was $\approx$ 4 s, 2 mAs per scan. The X-ray system based on a standard mammography system (Siemens Mammomat 300®) used an X-ray tube with Mo-anode and was tuned to 17.5 keV, i.e. the Mo Kα energy. Details can be found elsewhere. [13].

The advantages of such a system are that it is rather easy to realize and delivers a monochromatic spectrum with high energy resolution. Measurements at different phantoms, i.e. thin layers of various materials, contrast media-filled cuvettes, or anthropomorphic samples showed a contrast enhancement up to a factor of two, depending on the samples and spectra used (see Ref. [13] for details).

Nevertheless turning this setup into a product is a challenge. The system is a scanning system which has all the shortcomings discussed above (see Section 3). Since only a small fraction of the radiation with the right energy hits the slot, a high tube load is necessary, but only a small dose is delivered to patient and detector. This not only results in a long scan time, but several scans (some 20) have to be summed up to reach the total detector input dose which is required for a high-quality X-ray image.

5.7. Phase contrast imaging

X-ray imaging can, of course, make use of other physical properties of the matter under investigation apart from absorption. Especially low-Z materials with low absorption differ in their refractive index for X-rays. This will alter the phase and the direction of a ray passing the object. The detected phase differences allow discrimination of details which remain barely visible with conventional methods.

A couple of different methods have been developed which use phase information, e.g. Phase Sensitive Imaging (PSI), Phase Contrast Imaging (PCI), and Diffraction Enhanced Imaging (DEI). Coherent radiation is required for phase contrast. Therefore, the feasibility of these methods has been demonstrated in synchrotron experiments. An example for DEI by Pisano et al. [14] is given in Fig. 6. Nevertheless, a micro-focus X-ray tube delivers sufficiently coherent radiation, and even a mammography tube with $100\,\mu m$ focus also works at some distance. [15].

Phase contrast images show high contrast resolution and high spatial resolution. This is due to the fact that scattered radiation is effectively suppressed by the long distance between sample and detector, or also by the analyzer crystal. This might provide an opportunity for a dose reduction.

The challenge of phase contrast imaging is that synchrotrons are rarely available in clinical practice. Coherent X-ray beams with small-focus tubes might be a solution, but there is still the question whether after passing the monochromator and long distances sufficient intensity remains for fast imaging. The systems have to be in scanning geometry and, therefore, need long exposure time. Moreover, from the medical point of view image interpretation is not established. The images show lots of details which cannot be assigned easily to known lesions. Even if

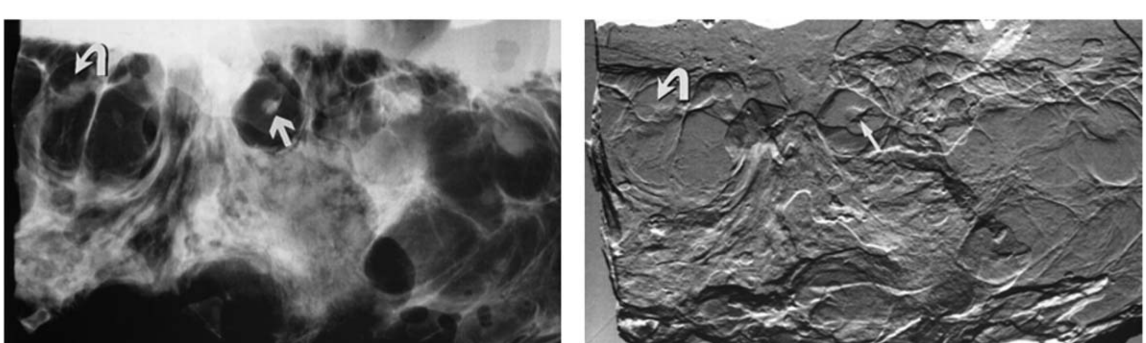

Fig. 6. In vitro infiltrating ductal carcinoma: common digital radiogram (left image) and diffraction enhanced image taken at 18 keV (right image). DEI enhances contrast of many details (from Ref. [14]).

phase contrast imaging is realized from the technical side, it will take a long time to establish this method for the radiologists.

5.8. Terahertz imaging

Terahertz imaging is a totally different method being discussed also for medical diagnosis. Electromagnetic Terahertz waves cover a frequency range of 0.1 – 30 THz, which means the quantum energy range 0.4 – 120 meV, or the wavelength range 3 mm to 10 μm, i.e. the far infrared (FIR).

Terahertz waves are strongly absorbed in water. Therefore, only the skin of a human body up to a depth of about 1 mm can be penetrated. This restricts its possible applications to dermatology and dentistry.

Moreover, Terahertz sources are costly. Possible methods require lasers and optical mixing or use photoconductive dipole antennas. Some experiments have been performed in the field of airport security to look through clothes. Unfortunately, THz waves will not even penetrate a soaked coat.

6. General trends in medical imaging

First of all, all images are becoming digital. Digitization takes place in an early state right behind the device, where the primary signal is generated. In the case of counting detectors, even the primary signal is of digital nature. Digital images offer the possibility of becoming easily processed, enhanced, displayed, transmitted, and archived.

3D methods are gaining preference over 2D because they are necessary to guide more and more complicated interventions (e.g. minimally invasive, intravasal). Most imaging methods hitherto have delivered only 2D images. Advanced systems have nowadays been started up and allow 3D data sets to be calculated from a series of single projections. Sophisticated algorithms have been developed for this purpose even in the case of non-ideal input data. The 3D images give the radiologist a much better orientation especially in the case of complicated interventions.

The combination of different modalities offers much more insight and enables a better diagnosis than images from a single modality. In most cases, one modality such as CT sets the anatomical landmarks, another modality contributes the functional information necessary.

Functional imaging will become more and more important for a precise investigation not only of the morphology, but of the processes going on in the human body. Time-dependent, dynamic measurements allow perfusion of the organs to be studied where any abnormal behavior can be quickly detected. Moreover, functional imaging aims at molecular methods which can be extremely specific and foster the vision of detecting cancer at a very early stage.

Last but not least, quantitative methods are becoming more established. The degree of a stenosis, for example, can be calculated from different projection images. Blood flow velocities or oxygen concentrations can be assessed. These quantitative methods are replacing the more or less qualitative images the radiologist has had up to now.

In the past medical X-ray imaging had mainly been used for diagnosis. Increasingly, imaging is necessary for therapy: image-guided interventions and operations are becoming state-of-the-art allowing individual treatments for every patient. 3D images in particular are used for therapy planning, and virtual reality offers us never-before-seen fly through impressions of the human body.

As a consequence of digitization, the connectivity of the whole health care system is becoming more a reality. Images are archived in picture archiving and communication systems (PACS) and are available wherever they are needed in a clinic, at a local physician, or at a private home. Tele-medicine decouples the place where an image is recorded from the place where it is assessed. From the technical point it is no longer difficult to consult a remote expert. Soon the electronic patient record will compile all radiological images and other medical data together avoiding unnecessary multiple examinations.

Finally, computer-assisted diagnosis (CAD) will help the radiologists by offering a second opinion which increases the sensitivity of their diagnosis.

In summary, the aim of today's medical imaging are a better diagnosis, a targeted therapy, cost optimization, and a milestone towards prevention.

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