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Advances in imaging from the first X-Ray images

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X-rays as well as other forms of radiation continue to play a crucial role in medical and experimental science. Thanks the development of sophisticated computer technology, it is now possible to combine thousands of 2D X-ray slices into a 3D image for greater accuracy in pinpointing the location of tumors, bone breaks, and other internal ailments of the human body. X-rays are also widely used outside of the medical field. The wavelength of X-rays is comparable to the size of atoms. Therefore, they are ideally suited for probing the structural arrangement of atoms and molecules in a wide range of materials. The sections of this review are presented in a logical order beginning with the discovery of X-rays, followed by selected experimental details, with the final sections covering diagnostic radiology physics and other, non-medical, applications. Roentgens story is widely known, but peoples who helped lay radiology's foundations remain essentially anonymous, especially to younger physicists and physicians.

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1. X-rays – Early History

The true start of imaging, medical and non-medical, as we consider it today was in 1895 when Roentgen discovered the X-ray in his Wurzburg laboratory on November 8. Almost immediately after Wilhelm Conrad Roentgen announced the discovery of the X-ray, imaging techniques based on the discovery were implemented all over the world.

For example, chest radiography became one of those early applications, even though the equipment seems crude by comparison to that of today, and certainly there was no knowledge of the potential deleterious effects of the ionizing radiation of X-rays. Roentgen's invention heralded the start of the modern era of medical imaging (Fig. 1).

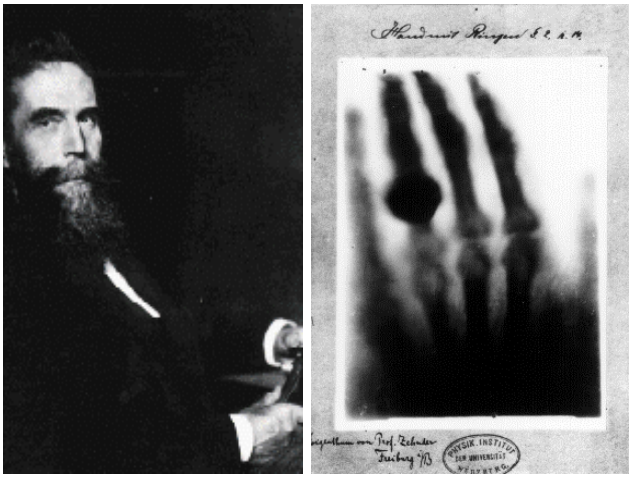

Fig. 1. Wilhelm Conrad Roentgen and by-then-famous X-ray image of his wife hand.

German physicist, a person who studies the relationship between matter and energy, Wilhelm Conrad Roentgen (1845–1923) discovered X-rays in 1895 while he was experimenting with electricity. Because he did not really understand what these rays were, he called them X-rays. By 1900, however, doctors were using X-rays to take pictures (called radiographs) of bones, which helped them treat injuries more effectively.

In 1901, Roentgen was awarded the first Nobel Prize for physics for his discovery of this short-wave ray. He donated all the prize money to his university. Keeping his will the newly discovered rays were called just X-rays ("x" is usually used to denote the unknown entity). He refused to take out patent on this discovery because he wanted the entire mankind to receive the benefits of X-rays. He even forbade naming of these rays after him. The reader can find historical details that describe events leading up to and occurring around the time of Roentgen's discovery in excellent articles by Linton [1], Assmus [2] and Mould [3], to say about few. Roentgen tested his new rays to define their properties and made numerous observations before writing a paper that was submitted for publication on December 28, 1895, to a local scientific publication [4]. Roentgens prestige in the community was such that his paper was accepted without review and published immediately [4].

Scientific American published in its new section a short bulletin headlined "Professor Roentgen's Wonderful Discovery" [5]. The first mention of the X-ray in *Science* magazine was a brief latter in the issue of January 31, 1896, from Hugo Munsterberg, a Harvard University physics professor [6]. *Nature* published a full translation of Roentgens paper [7].

Roentgen was dominated by a shyness that made him evade personal contacts wherever he could. In a brief period of time that follows, the X-ray went from a physics experiment to almost routine medical practice.

One can see what could be achieved in physics before the occurrence of the technological revolution involving not only computer applications but also the disappearance of the small independent X-ray companies into today's multinational companies. Research and development is nowadays just too expensive for much independent practical high-technology contributions without financial backing.

2. The use of X-rays for analysis

X-rays are electromagnetic radiations having wavelengths roughly within the range from 0.05 to 100 Angstroms. Their similarities to light led to the tests of established wave optics: polarization, diffraction, reflection and refraction. Despite limited experimental facilities Roentgen could find no evidence of these. May be, it was additional reason he called them "x" rays.

For diffraction applications, only short wavelength X-rays (hard X-rays) in the range of a few Angstroms to 0.1 Angstrom (1 keV - 120 keV) are used. Because the wavelength of X-rays is comparable to the size of atoms, they are ideally suited for probing the structural arrangement of atoms and molecules in a wide range of materials. The energetic X-rays can penetrate deep into the materials and provide information about the bulk structure.

This year marks the 100th anniversary of the discovery of X-ray diffraction and its use as a probe of the structure of matter [8-11]. Sixteen years after Wilhelm Conrad Rontgen announced in 1895 his discovery of "X" rays that can penetrate the body and photograph its bones, Max von Laue, a professor of physics at the University of Munich in Germany, worked on a theory of the interference of light in plane parallel plates. Laue was Plank's favorite disciple. His interest covers the whole of physics. If, as some argued, X-rays were not made up of particles but were a form of electromagnetic radiation similar to ordinary (visible) light, and then it should be possible to repeat well-known optical experiments using X-rays instead of beams of ordinary light.

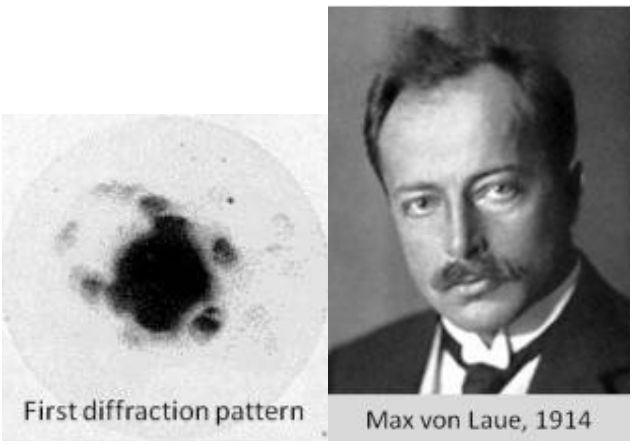

Fig. 2. Max von Laue and the first diffraction pattern.

In 1911, von Laue suggested to one of his research assistants, Walter Friedrich, and a doctoral student, Paul Knipping that they try out X-rays on crystals. His reasoning was that X-rays have a wavelength similar to the inter-atomic distances in crystals, and as a result, the crystal should act as a diffraction grating. Von Laue, always the theoretician, did not actually make the necessary experiments. In a single elegant experiment performed by Friedrich and Knipping, von Laue had proven the wave-like nature of X-rays and the space-lattice structure of crystals at the same time (Fig. 2) [8,9]. When he received the Nobel Prize for what the Committee said was his "epoch-making discovery", Max von Laue gratefully acknowledged Friedrich and Knipping for their roles in the discovery; and for him it went without saying that he shared his prize money with them [10,11]. Einstein hailed von Laue's discovery as one of the most beautiful in the history of physics.

Before the Laue experiment, did anyone dream of tools allowing one to explore the structure of matter on the molecular scale and use this information for deriving structure–property relationships of materials – or for understanding the molecular basis of life? After X-rays had already been used to image the internal anatomy of the human body, with the Laue experiment the internal structure of crystals also became accessible on nanoscale [11].

Laue's pioneering work in X-ray crystallography opened the way for two, quite different, developments in physics, both of them of immense importance. First, it confirmed the electro-magnetic nature of X-radiation and made it possible to determine the wavelength of X-rays with great accuracy. Second, it gave physicists and chemists a new tool for investigating the atomic structure of matter. In the 1950s it was X-ray diffraction studies that enabled scientists to reveal the structure of the nucleic acids (DNA and RNA) and to establish the new discipline of molecular biology.

English physicists Sir William Henry Bragg and his son, Sir William Lawrence Bragg (Fig. 3) argued that when the X-rays are reflected off two successive planes of atoms in the crystal, they interfere constructively if the difference in the distance traveled is equal to an integral number of wavelengths. Thus the famous Bragg condition is

$$n\lambda = 2d\sin\theta .$$

They have developed the above relationship to explain why the cleavage faces of crystals appear to reflect X-ray beams at certain angles of incidence (θ) [12]. The variable d is the distance between atomic layers in a crystal, and the variable λ is the wavelength of the incident X-ray beam; n is an integer. This observation is an example of X-ray wave interference, commonly known as X-ray diffraction (XRD), and was direct evidence for the periodic atomic structure of crystals. By 1913, just a year after they had pioneered the method, crystal analysis with X-rays had become a standard method. The results gave insight into the structure of crystals. The Braggs were

awarded the Nobel Prize in physics in 1915 for their work in determining crystal structures beginning with NaCl, ZnS and diamond [2, 11-13].

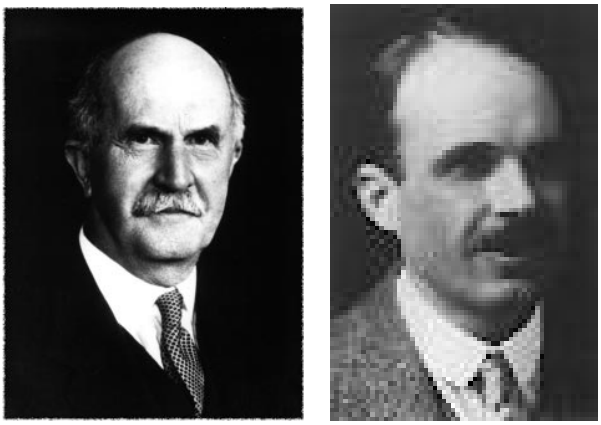

Fig. 3.Sir William Henry Bragg and Sir William Lawrence Bragg.

Bragg's law describes the mechanism by which X-ray diffraction occurs and was an extremely important discovery - it formed the basis for what is now known as crystallography (Fig. 4).

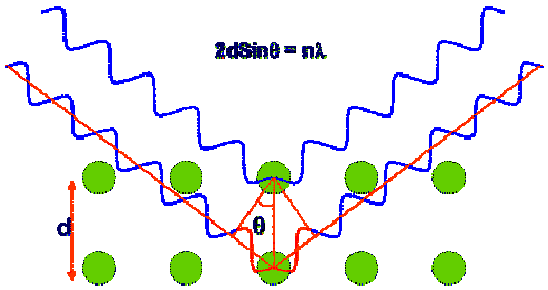

Fig. 4. Bragg's law: two-dimensional representation. An incident X-ray beam interacts with the atoms arranged in a periodic manner. The atoms (green spheres) can be viewed as forming different sets of planes in the crystal (colored lines). For a given set of lattice planes with an inter-plane distance d *, the condition for a diffraction to occur can be simply written* $2d \sin\theta = n\lambda$ *. In the equation,* λ *is the wavelength of the X-ray,* θ *is the scattering angle and* n *is the order of interference.*

X-rays primarily interact with electrons in atoms. When X-ray photons collide with electrons, some photons from the incident beam will be deflected away from the direction where they originally travel. If the wavelength of these scattered X-rays did not change (this means that X-ray photons did not lose any energy), the process is called elastic scattering in that only momentum has been transferred in the scattering process. These are the X-rays that one measure in diffraction experiments, as the scattered X-rays carry information about the electron distribution in materials. On the other hand, in the inelastic scattering process, X-rays transfer some of their energy to the electrons and the scattered X-rays will have different wavelength than the incident X-rays.

Diffracted waves from different atoms can interfere with each other and the resultant intensity distribution is strongly modulated by this interaction. If the atoms are arranged in a periodic fashion, as in crystals, the diffracted waves will consist of sharp interference peaks with the same symmetry as in the distribution of atoms. Measuring the diffraction pattern therefore allows us to deduce the distribution of atoms in a material. The peaks in an X-ray diffraction pattern are directly related to the atomic distances.

In the same year Moseley showed the wavelengths were not only characteristic of the element the target was made of, but also they had the same sequence as the atomic numbers. This allowed atomic numbers to be determined unambiguously for the first time.

X-ray crystallography is a standard technique for solving crystal structures. Its basic theory was developed soon after X-rays were first discovered more than a century ago. Over the years that follow it has gone continual development in data collection, instrumentation and data reduction methods. In recent years, the advent of synchrotron radiation sources, area detector based data collection instruments, and high speed computers has dramatically enhanced the efficiency of crystallographic structural determination. Synchrotron radiation is emitted by electrons or positrons traveling at near light speed in a circular storage ring. These powerful sources, which are thousands to millions of times more intense than laboratory X-ray tubes, have become indispensable tools for a wide range of structural investigations and brought advances in numerous fields of science and technology.

Today X-ray crystallography is widely used in materials and biological research.

In X-ray crystallography, integrated intensities of the diffraction peaks are used to reconstruct the electron density map within the unit cell in the crystal. To achieve high accuracy in the reconstruction, which is done by Fourier transforming the diffraction intensities with appropriate phase assignment, a high degree of completeness as well as redundancy in diffraction data is necessary, meaning that all possible reflections are measured multiple times to reduce systematic and statistical error. The most efficient way to do this is by using an area detector. The latter can collect diffraction data in a large solid angle.

The most common use of powder (polycrystalline) diffraction is chemical analysis. This can include phase identification, investigation of high (low) temperature phases, solid solutions and determinations of unit cell parameters of new materials. The crystalline inclusions in inorganic & organic polymers give sharp narrow diffraction peaks and the amorphous component gives a very broad peak (halo). The ratio between these intensities can be used to calculate the amount of crystalline phase in the material.

Nowadays, X-ray diffraction (XRD) allows a range of determinations to be made including phase identification of crystalline materials, phase quantification, glass content and quality control methods, to say about few.

Soon after it was also established that secondary fluorescent X-rays were excited in any material irradiated with beams of primary X-rays. This started investigation into the possibilities of fluorescent X-ray spectroscopy as a means of qualitative and quantitative elemental analysis.

3. Industrial Radiology

X-rays are also used extensively in industry as a non-destructive testing method that examines the volume of a specimen. Radiographs of a specimen showed any changes in thickness, internal and external defects, and assembly details invisible to the naked eye.

4. Airport Security

In the 1960s, X-ray screening machines were introduced alongside metal detectors at airports to detect bombs in luggage. Since then, they've become a standard fixture not only in airports, but in many government buildings.

Security scanners are a valuable alternative to existing screening methods and an effective method of screening passengers as they are capable of detecting both metallic and non-metallic items carried on a person. The scanner technology is developing rapidly and has the potential to significantly reduce the need for manual searches applied to passengers, crews and airport staff.

In order not to risk jeopardizing citizens' health and safety, only security scanners which do not use X-ray technology are added recently to the list of authorized methods for passenger screening in EU-countries airports.

5. Risk Factor

Exposure to X-rays may cause cancer at high-enough levels. Because it does take a long time for this damage to happen, X-rays were not immediately suspected as the cause. The first recorded death from X-ray radiation damage was Clarence Dally, one of Thomas Edison's assistants. Through the first half of the Twentieth Century, intensive research was done into the effects of this radiation, and protective measures (such as lead shielding) developed to reduce exposure to it.

Undoubtedly, the early detection of health problems is very important. Over the last decades, various imaging techniques such as X-rays, computed tomography and magnetic resonance scans have been developed and applied to diagnostic, as well as therapeutic medical care.

However, in recent years, physicians have become concerned with the overuse of certain diagnostic techniques, in particular those that expose patients to radiation. Although infrequent use of X-ray or computed tomography scans will not have adverse effects on a patient, multiple exposures to radiation over a short period of time can cause serious damage to cells, resulting in an increased risk of cancer and other diseases.

6. The use of X-rays for Medical Purposes

6.1. Retrospective glance

The medical community immediately recognized and continuously developed the extraordinary potential of X-rays for diagnostic purposes. Physicians reading about seeing bones on X-rays were quick to perceive medical applications. Edwin Frost's physician brother brought him the patient with a fractured ulna who received the first documented U.S.A. medical X-ray [1]. In the decades following, several applications demonstrated for the first time the ability to look inside the body without dissection to study internal anatomy. Over the years there have been significant improvements in the X-ray technique, primarily due to the higher sensitivity and fidelity of the recording films, not necessarily any significant advances in the basic methodology.

This section attempts to briefly summarize the history of visualizing the internal body for medical, with primary focus on present capabilities. A few predictions will be made by extrapolating from present to possible future advances. Copious citations will not be used, as most of this treatise is based on 4 decades of personal opinion and experience as well as the topics included in this perspective – past, present and future.

If we focus on the historical evolution of medical imaging alone, leaving aside for now the significant parallel advances in biological imaging facilitated by the invention of the microscope, the field dates back to the early parts of the 12^{th} and 13^{th} centuries with direct visualization by dissection in anatomy theaters. This was the principal form of imaging that is direct visualization via dissection, for almost 600 years until near the end of the 19^{th} Century when a form of imaging was introduced to aid visualization into the body without dissection – namely the discovery of the X-ray. The sensitivity and quality of recordings by this technique improved over the next several decades.

For many years after the discovery of X-rays, X-ray fluoroscopic examinations were performed in a dark room by observing images on a fluorescent screen that glowed in response to X-rays that had passed through the patient's body. A major step forward in fluoroscopy was made by replacing the fluorescent screen with an electronic instrument based on television technology in the 1950s. This leads to a significant increase in image brightness. In the 1980s, digital subtraction angiography (DSA) was introduced in the field of vascular contrast studies. In DSA, analog video signals from a TV camera are converted to digital data, and vascular structures are clearly demonstrated through digital processing and subtraction of non-vascular anatomy. Subsequently, rapid advances in computer technology resulted in a wider range of diagnostic applications.

Since its inception, fluoroscopy has, and continues to be a key imaging modality used in interventional radiology,

a branch of radiology that is concerned with the use of image guidance to conduct minimally invasive procedures for both diagnostic and therapeutic purposes. These procedures include angiography, angioplasty, pacemaker insertion and embolization, to say about few. The reason X-ray fluoroscopy remains a dominant imaging modality in interventional radiology is because no other single modality provides the same combination of high spatial and temporal resolution which is particularly important for proper deployment of endovascular (from within the blood vessel) devices such as stents or coils. However, the harmful effects of ionizing radiation used in fluoroscopy, which have long been recognized, require the patient dose to be as low as reasonably achievable during an intervention. This is often referred to as the ALARA principle. The use of harmful X-ray radiation is justifiable by considering that the benefit from the clinical outcome of the intervention will outweigh the adverse biological effects of the radiation.

These biological effects include indirect and direct effects.

Indirect effects of ionizing radiation arise when electrons set in motion by X-ray photons excite and ionize water molecules, creating free radicals which then cause damage to critical biological targets such as DNA.

In **direct effects**, electrons directly ionize DNA molecules. As a result, in certain cases such as pediatric interventions, a particularly strict adherence to ALARA is required, since the accrued stochastic effects due to radiation exposure are more likely to disrupt tissue growth and development as well as lead to an increased chance of cancer over the child's lifetime. There are adverse effects associated with other imaging modalities as well. The electromagnetic radiofrequency pulses used in MRI are known to cause heating. This can be particularly problematic near metallic devices or implants such as pacemakers or hearing aids. Ultrasound contrast agents, when exposed to ultrasound waves, can also cause potential bio-effects (i.e. rupture of cell membranes) at the level of the microcirculation, although the clinical relevance of such bio-effects remains unclear.

6.2. Clinical fluoroscopy requirements for interventional radiology

A modern fluoroscope consists of a large "C" shaped mount called a C-arm with an x-ray source on one end and an x-ray imager on the other. This assembly can be positioned such that different projections of the patient anatomy may be acquired from different angles. In certain cases, the C-arm assembly is rotated around the patient during injection of a contrast dye and multiple projection images are acquired and subsequently reconstructed into a three-dimensional rendition of the vasculature. The C-arm assembly should hence be designed such that the x-ray source and x-ray imager are as small and light as possible to facilitate its positioning or rotation and to improve patient accessibility.

In the fluoroscopic mode, the physician typically guides interventional devices such as guide wires or stents through a catheter towards the lesion and is mainly concerned with tracking the position of the device. This guidance, usually referred to as a ***catheterization***, is typically done at relatively high imaging frame rates (7.5 – 30 image frames per second) so that the physician can get a good sense of the advancement of the device towards the lesion while avoiding potential complications due to, for example, arterial tortuosity. Catheterization is often a relatively time consuming process (ten minutes or longer) and is done at very low X-ray exposures (mean exposure of 1 μR per frame at the imager) to minimize patient radiation exposure. The X-ray exposures employed are so low, in fact, that quantum noise (the stochastic variation in the spatial distribution of X-ray photons) becomes the dominant form of noise in the fluoroscopic images obtained using an XRII system. Because the interventional device being imaged typically has a high degree of radio-opacity, these low exposures are often adequate to obtain sufficient contrast to image the device. In the cine mode, sequences of images are acquired during administration of an X-ray contrast agent (typically via a catheter) into the vasculature. These relatively short (several seconds in duration) image acquisitions are taken at higher exposures (~10 μR per frame) so as to provide superior image quality (less quantum noise) and thus improve the diagnostic value of the images. This mode is also used when accurate positioning or deployment of endovascular devices is performed. In the radiographic mode, images are acquired at even larger exposures (~100 μR per frame) for applications such as digital subtraction angiography (DSA) which have been shown to improve the detection of certain lesions such as aneurysms or thrombi.

High spatial resolution is an important requirement in the cine and radiographic imaging modes, as it can strongly affect the diagnosis or treatment outcome of an interventional procedure. Interventional devices such as guide wires or stenos typically have wire diameters ranging from 50-200 μm. It has been demonstrated that despite the effects of x-ray scattering, imaging of individual stenos wires (struts) using a high resolution imager is possible inside a human head phantom; this should enable the deployment of novel asymmetrical stenos for specialized therapeutic neurovascular applications. Furthermore, in certain applications such as coronary angiography, detection of small calcium deposits (tens of micrometers in size) in coronary arteries provides an important means of assessing the degree of atherosclerosis as well as the likelihood of a successful angioplasty. For optimal imaging of fine features in interventional radiology, the imager should be able to resolve 5 line pairs per millimeter (a line pair is a pair of light and dark lines) such that the relative contrast between the two lines of each pair is greater than 0.2 (i.e. a modulation transfer function (MTF) greater than 0.2 at a spatial frequency of 5 cycles per mm).

From the discussion above, it follows that the key requirements for a clinical X-ray imager for interventional radiology – beyond a thin profile and providing unobstructed access to the patient - are:

(1) quantum-noise limited (QNL) operation at the lowest clinical fluoroscopic x-ray exposures (in conformance with the ALARA principle);

(2) capability for modes of operation that require significantly higher x-ray exposures and

(3) capability of imaging fine features of interventional devices or lesions.

The imager should also be able to operate at up to 30 frames per second.

6.3. X-ray image intensifiers

Until recently, the most widely used X-ray imaging system in interventional radiology was the X-ray image intensifier (XRII). This is an electro-optical device that operates inside a vacuum enclosure (Fig. 5(a)) which contains an input phosphor used to convert X rays into optical photons. The phosphor is coupled to a photocathode which, upon exposure to these optical photons produces electrons. The latter are accelerated in an electric field and hit an output phosphor screen. This process enables the production of several thousand optical photons for each photoelectron emitted from the photocathode. The resulting optical image is captured using an optical assembly and a video camera or charge coupled device (CCD). XRII/video systems provide excellent X-ray sensitivity (the degree to which small numbers of X rays - ideally a single X ray - can be detected) due to the large internal gain of the XRII, however, the XRII also presents important limitations. These are associated with the curvature of the input phosphor and the presence of multiple conversion stages, leading to geometrical distortions (particularly in the periphery of the images), spatial non-uniformities and a degradation of the imaging resolution. Furthermore, these systems are bulky and heavy (they can weigh several hundred pounds), compromising patient accessibility and image acquisition modes such as rotational angiography or cone-beam computed tomography. Another important limitation of the XRII is its high sensitivity to magnetic fields (including the earth's magnetic field) which produces a distortion in the image that is shaped like an "S" and referred to as an S-distortion.

Due to these substantial limitations and the availability of new solid-state technologies, there has been a progressive trend in the past few years to replace XRII systems with flat panel detectors.

6.4. Flat panel detectors

There has been much work over the last decades on the development of solid-state flat panel detectors, also known as active matrix flat panel imagers (AMFPI). Unlike the XRII, these systems are thin, produce negligible spatial distortions and are insensitive to magnetic fields. In principle, panels with sufficiently small pixels, or *detector elements* also have the potential for substantially improved spatial resolution in comparison with the XRII because there are considerably less conversion stages involved in the image detection process (Fig 5 (b) and (c)).

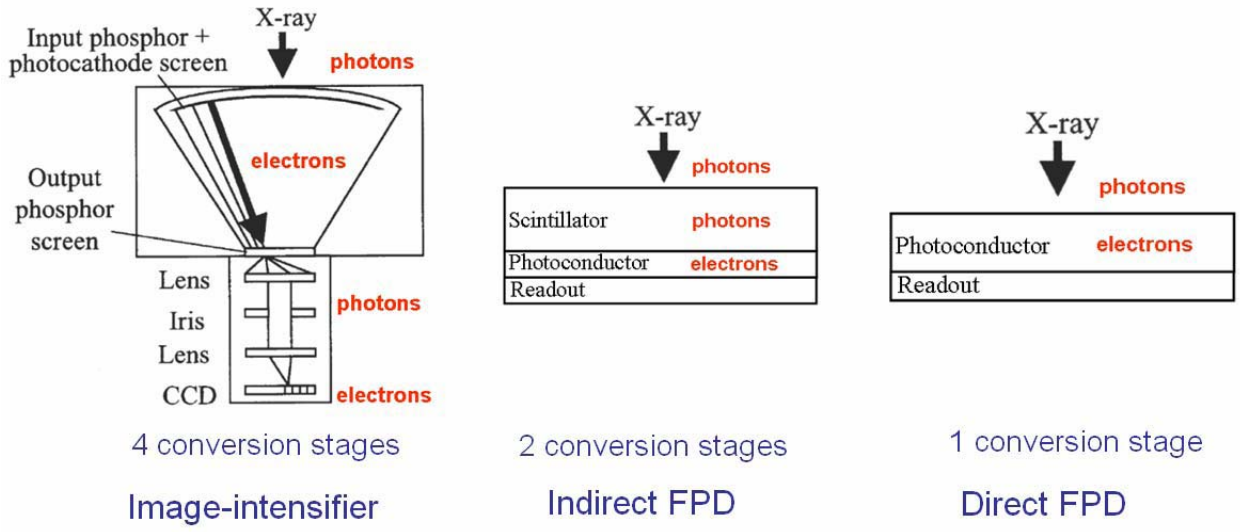

Fig. 5. Different types of X-ray imaging systems. (a) The image intensifier consists of an input phosphor coupled to a photocathode which converts X-rays into optical photons and subsequently electrons. The latter are accelerated in an electric field and hit an output phosphor screen. This produces an amplification of several thousand. The resulting optical image is captured using an optical assembly and a charge coupled device (CCD). (b) The indirect active matrix flat panel imager (AMFPI) consists of a scintillator which converts X rays into optical photons, a photoconductor which converts them in turn to electrons and a readout layer which stores and processes the resulting charge image. (c) In the direct conversion flat panel detector, X-rays are directly converted into charge inside a photoconductor. In each diagram, the electric field lines are shown as two lines next to an arrow which shows the direction in which the charge travels.

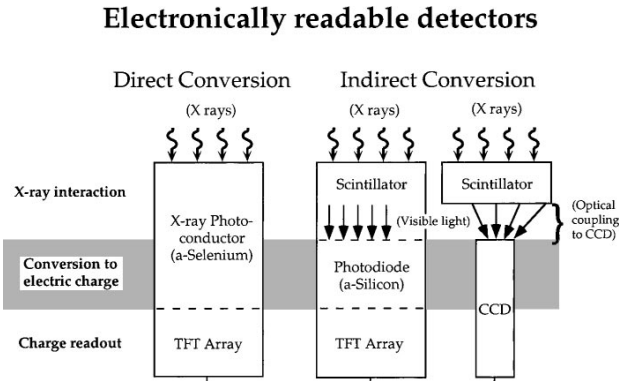

Fig. 6. Electronically readable detectors.

The majority of commercial AMFPIs are indirect conversion detectors, in which X-ray photons strike a scintillator such as cesium iodide (CsI) and generate optical photons which then interact with a photo-sensor (usually an amorphous silicon photodiode), in turn producing electron-hole-pairs (EHP) that are stored prior to being electronically processed (Fig. 5). The process of detecting the photon-generated charge from each del (referred to as readout) produces a digital image which represents the original distribution of X-rays incident at the imager's surface. In another class of detectors know as direct-conversion detectors, X-rays interact with a photoconductor, usually amorphous selenium (a-Se), and directly generate EHPs, which follow the parallel field lines in the presence of an electric field prior to being read out. Because there is no intermediary optical stage to contribute to blurring, these systems have the important advantage of providing superior spatial resolution compared to indirect AMFPIs, however, the photoconductor needs to be thick enough (~1000 μm) to yield a reasonable quantum efficiency at radiographic X-ray energies (20 – 150 kV). The very high spatial resolution of direct-conversion a-Se detectors has recently increased their use in digital mammographic imaging systems. Direct-conversion detectors are also being considered for use in tomosynthesis, in which a series of breast radiographs are acquired from different angles and reconstructed into a series of slices. In contrast with mammography, the image slices produced by tomosynthesis are largely immune to structural noise, which is the noise introduced into an image due to X-ray attenuation in overlapping anatomical structures. Most important applications of flat panel X-ray imagers (FPXIs) are in medical imaging such as mammography, chest radiology, angiography, fluoroscopy, etc.

Conversion of X-rays to images, parameters for digital imaging and properties typical for selected X-ray photoconductors used in large area applications are summarized in Table 1-3. Figs. 6 to 8 exemplify FPXI, a simple pixel with TFT and typical X-ray images, correspondingly.

Table 1. Conversion of X-rays to Images – comparison of different methods

Regime	**Detection method**	**Detector**	**Conversion from X-rays to Image**
Digital	Direct	Flat panel detector (amorphous Selenium)	X-rays → image
Digital	Indirect	Flat panel detector (fluorescent material + + photo diode)	X-rays → light→ image
Digital	Indirect	I.I.* + TV camera	X-rays → light→ image
Digital	Indirect	Imaging plate	X-rays → latent image→ → light→ image
Analog	Indirect	I.I.* + cine film	X-rays → latent image→ → light→ image
Analog	Indirect	Intensifying screen + + X-ray film	X-rays → latent image→ → light→ image

(I.I.* - Image Intensifier)

Table 2. Parameters for Digital X-ray Imaging Systems.

Clinical Task →	**Chest Radiology**	**Mammography**	**Fluoroscopy**
Detector size	35 cm × 43 cm	18 cm × 24 cm	25 cm × 25 cm
Pixel size	200 μm × 200 μm	50 μm × 50 μm	250 μm × 250 μm
Number of pixels	1.750 × 2.150	3.600 × 4.800	1000 × 1000
Readout time	~ 1s	~ 1s	1/30 s
X-ray spectrum	120 kVp	30 kVp	70 kVp
Mean exposure	300 μR	12 mR	1 μR
Exposure range	30 – 300 μR	0.6 – 240 mR	0.1 – 10 μR
Radiation noise	6 μR	60 μR	0.1 μR

*The **pixel** (a word invented from "picture element") is the basic unit of programmable color on a computer display or in a computer image.

Table 3. Properties typical for selected X-ray photoconductors used in large area applications [15].

Photoconductor **State** **Preparation**	**δ** at 20 keV **δ** at 60 keV	$\mathbf{E_g}$ eV	$\mathbf{W_{\pm}}$ eV	**Electron** $\mu_e\tau_e$ (cm^2/V)	**Hole** $\mu_h\tau_h$ (cm^2/V)
Stabilized a-Se Amorphous Vacuum deposition	49 μm 998 μm	2.2	45 at 10 V/ μm 20 at 30 V/ μm	3×10^{-7} – 10^{-5}	10^{-6}– 6×10^{-5}
HgI_2 Polycrystalline PVD	32 μm 252 μm	2.1	5	10^{-5}–10^{-3}	10^{-6}–10^{-5}
HgI_2 Polycrystalline SP	32 μm 252 μm	2.1	5	10^{-6}–10^{-5}	10^{-7}
$Cd_{95}Zn_{0.5}Te$ Polycrystalline Vacuum deposition	80 μm 250 μm	1.7	5	2×10^{-4}	3×10^{-6}
PbI_2 Polycrystalline Normally PVD	28 μm 259 μm	2.3	5	7×10^{-8}	2×10^{-6}
PbO Polycrystalline Vacuum deposition	12 μm 218 μm	1.9	8-20	5×10^{-7}	small
TlBr Polycrystalline Vacuum deposition	18 μm 317 μm	2.7	6.5	small	$1.5\text{-}3\times10^{-6}$

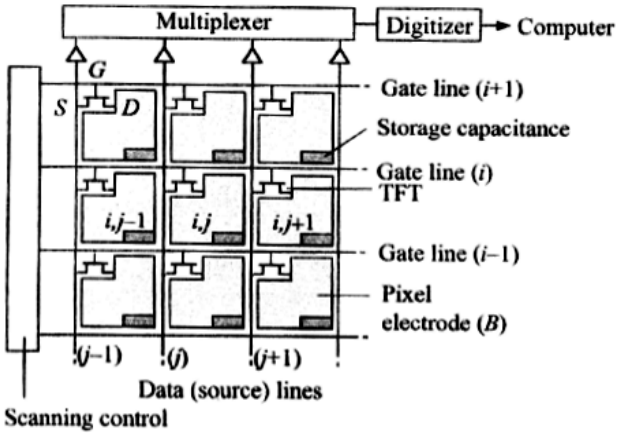

Fig. 7. A simplified schematic illustration of a FPXI and its peripheral electronics (see [15] for details &Ref's therein).

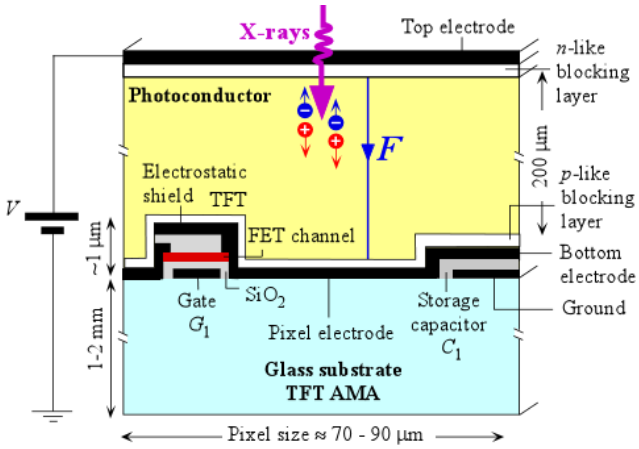

Fig. 8. A simplified schematic diagram of the cross section of a simple pixel with thin film transistor (TFT) [15].

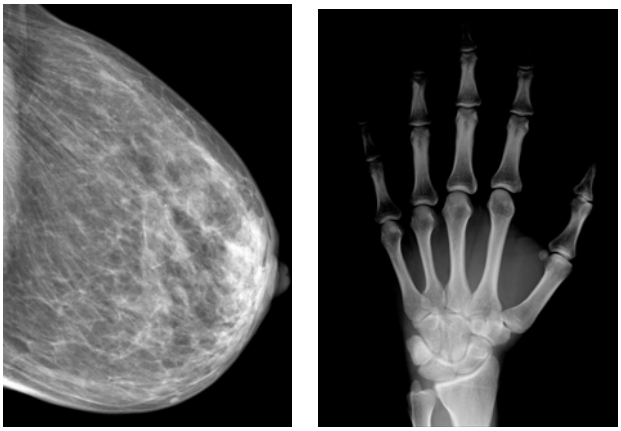

Fig. 9.Two typical X-ray images from an amorphous Se (a-Se). Left, a typical X-ray image of a breast. Right, an X-ray image of a hand [15].

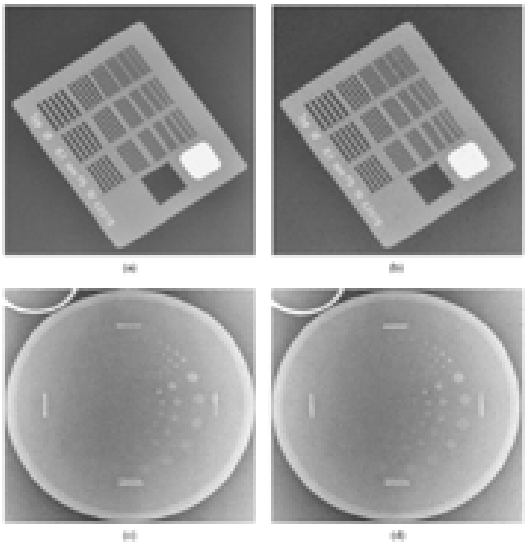

Fig. 10. Effect of pixel loss on image quality.

7. A new revolution in optical imaging

Although improvement in recording media considerably enhanced the quality and use of X-rays for medical purposes, with the notable exception of fluoroscopy and nuclear imaging developed decades later, it was not until the early 1970s that a new revolution began in medical imaging.

The era of modern medical imaging did not begin until the 1970s. This modern era was heralded again by an X-ray imaging device called the "CAT" scanner or Computerized Axial Tomograph device, which has long since been called simply Computed Tomography, or CT. This device contributed three major significant features to medical imaging that continues to be its foundation today: 1) the image was digital, produced by a computer, and could be readily modified, analyzed and displayed by computers, 2) the method provided sensitivity to tissue density differences unattainable theretofore, and 3) the methodology provided cross-sectional views of the human body, eventually multiple cross-sectional views adjacent one to another, providing a three dimensional view of internal anatomic structures. Since the body is 3D and the organs have different shapes, sizes and positions relative one to another in 3D space, imaging adjacent thin body cross sections was an important advance in medicine's ability to more accurately see and understand the true nature of objects inside the body.

Soon after the advent of this scanner in the 1970s, 3D imaging became available and other modalities began to be rapidly developed. Particular note is given to magnetic resonance imaging (MRI) in the early 1980s because of its near revolutionary impact on soft tissue imaging. Nuclear systems, notably positron emission tomography (PET), introduced functional imaging, followed by high-speed CT (helical) and rapid MR imaging (fMRI). By the decade of the 1990s, with significant performance gains in imaging

methodologies, interactive multi-dimensional, multi-modality imaging for improved diagnosis, treatment, guidance and therapy monitoring became routine in large medical centers. The turn to the 21st Century was characterized by the advent of many image-guided interventions, often associated with minimally invasive surgery, for planning, rehearsal and execution of a wide variety of clinical and surgical procedures.

The continuing goals for development and acceptance of important visualization display technology are: (a) improvement in speed, quality and dimensionality of the display and (b) improved access to the data represented in the display through interactive, intuitive manipulation and measurement of the data represented by the display. Included in these objectives is determination of the quantitative information about the properties of anatomic tissues and their functions that relate to and are affected by disease. With these advances in hand, the delivery of several important clinical applications will soon be possible. Major events in diagnostic imaging are given in Table 4.

Table 4. Major events in diagnostic imaging over the last five decades.

1950s	Utilization of an image-intensifier system for fluoroscopy Development of a gamma camera for radionuclide imaging
1960s	Development of a 90 s automated film processor Basic research on image quality, MTFs, Wiener spectra and quantum mottle
1970s	Development of rare-earth screen-film system, digital subtraction angiography (DSA), computed tomography (CT), ultrasound imaging with electronic scan Initial research on ROC analysis, MRI, PET, SPECT, PACS and electronic imaging
1980s	Development of computed radiography (CR), magnetic resonance imaging (MRI), color Doppler ultrasound imaging Initial research on computer-aided diagnosis (CAD)
1990s	Commercialization and clinical use of CAD system, flat-panel detector (FPD) systems, multi-detector computed tomography (MDCT), magnetic resonance angiography (MRA), harmonic/contrast imaging
2000s	Development and clinical use of real-time 3D ultrasound imaging, cone-beam CT, parallel MRI, PET/CT, full-field digital mammography (FFDM), MDCT with 256 detectors, molecular imaging and PACS

For CT scan and MRI, the comparison chart is given in Table 5.

These significant advances have set the stage for an exciting future that will include highly sensitive and specific imaging, real-time and multi-dimensional imaging, whereby almost any number of multiple orthogonal image variables can be fused and synchronized together to bring all collected information synergistically to bear on diagnosis and treatment of disease. The near future will demonstrate highly integrated capabilities for structural and functional information synchronously across space and time, and this will drive the practice of medicine of the future toward truly synchronous, minimally invasive, highly specific, highly sensitive and highly effective diagnosis and treatment of disease.

Table 5. CT Scan & MRI : Comparison chart.

	CT Scan	MRI
Principle :	X-ray attenuation was detected by detector and DAS system follow by math. model to calculate the value of pixelism then became a image	Makes use of the fact that body tissue contains lots of water (and hence protons) which gets aligned to large magnetic field to produce net MDM vector. The decay of MDM is detected as MR signal
Details of soft tissues	Less tissue contrast compared to MRI	Much higher detail in the soft tissues
Details of bony structures	Provides good details about bony structure	Less detailed compared to CT scan
Ability to change the imaging plane without moving the patient	With capability of MDCT after helical scan with Mlti- plan Reformation function, operator can construct any plane	MRI machines can produce images in any plane
Principal used for imaging	Uses X-rays for imaging	Uses large external field RF pulse and different gradient fields
Effects on the body	Despite being small, CT can pose the risk of irradiation	No biological hazards have been reported with the use of the MRI
Acronym for	Computed tomography	Magnetic Resonance Imaging
Scope of application	CT can outline bone inside the body very accurately	MRI is more versatile then the X-ray and used to examine a large variety of medical conditions
Cost	CT Scan costs range from $ 1.200 to $ 3.200; they usually cost less than MRIs	MRI costs range from $ 1.200 to $ 4.000 (with contrast); which is more than CT scans and X-rays and most examining methods
Radiation exposure	Moderate to high radiation	None
Time taken for complete scan	Usually completed within 5 minutes	Scanning typically run about 30 minutes
Disadvantages	Uses ionizing radiation	• More scanning time • Patient with metallic implants are not recommended * Patient with phobia required to give anesthesia during scan
Application	Suited for bone injuries Lung and Chest Imaging, cancer detection	Suited for ligament and tendon injury, spinal cord injury, brain tumors
Image specifics		Demonstrate subtle differences between the different kinds of soft tissues

Summing up the above, the key clinical requirements for a solid-state X-ray imager for interventional radiology are:
(1) quantum-noise limited (QNL) operation at the lowest clinical fluoroscopic x-ray exposures (in conformance with the ALARA principle);
(2) capability for modes of operation that require significantly higher x-ray exposures;
(3) capability of imaging fine features of interventional devices or lesions.
No existing solid-state imaging system simultaneously satisfies all three requirements.

Avalanche multiplication of charge in a-Se is the only that can provide sufficient gain to satisfy requirement (1) and the highly adjustable avalanche gain should also satisfy requirement (2). Furthermore, the high intrinsic imaging resolution of a-Se should also answer requirement (3) [15].

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