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Current studies and future perspectives of synchrotron radiation imaging trials in human patients

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ABSTRACT

The coherent and monochromatic x-ray beams available at the synchrotron radiation (SR) laboratories are ideal tools for the development and the initial application of new imaging techniques. In the present paper the history of the clinical studies in k-edge subtraction imaging with SR is summarized, including coronary angiography and bronchography. The results of the recent trial in phase-contrast mammography at Elettra (Trieste, Italy) are discussed, in order to assess the clinical impact of the new imaging modality and the potential interest in its translation to clinical practice. The direct measurement of linear attenuation coefficient obtained during the SR mammography trial is also discussed.

The new program of phase-contrast breast CT under development at Elettra is presented. Recently, 3D breast imaging (tomosynthesis and cone beam breast CT) has been introduced in clinical practice with significant improvement in diagnostic accuracy. The aim of this research is to study the contribution of the phase-contrast to the image quality of breast CT.

Increasing the image quality of the x-ray medical images at the level of the results obtained at the SR laboratories is highly desirable, hence the promising techniques for the translation of the phase-contrast imaging to the hospitals are briefly discussed.

1. Introduction

It is well known that the object of the first radiograph was the hand of Mrs. Rontgen in 1895. Recently the radiographs of another hand have been published and the contrast mechanism in these new images is no longer based on x-ray attenuation [1]. Between these images there is more then one century of physics, radiology and technical developments. In the present paper a recent and fascinating chapter of this story will be discussed: medical imaging with synchrotron radiation (SR). The new hand radiographs, obtained using a conventional x-ray generator, may be considered as a result of researches done in medical imaging with SR and therefore will be discussed in the last section of the present paper.

During the XX century new imaging modalities based on ultrasound and nuclear magnetic resonance have been developed and are used in clinical practice. However x-ray imaging still has a fundamental role in medical imaging: digital detectors, tomographic techniques, and image processing tools create detailed views of the organs inside the human body. On the contrary the technology of x-ray sources for medical imaging is almost unchanged since the development of the rotating anode x-ray generator in 1898. One of the main constrains of medical imaging is the short acquisition time. In human body, there are a number of organs that are moving and that can not be voluntary stopped. The heart for instance is an excellent example. The average cardiac frequency is about 60 Hz, consequently in principle, each radiograph should be acquired in less than 1 s. Accordingly, x-ray sources suitable for medical imaging have to produce high flux, putting into consideration the thickness of the human body and the x-ray attenuation coefficients of its components. The success of the rotating anode in radiology is due to the capability of the system to obtaining short exposure time and high flux without damaging the anode surface. On the other side the improvement of x-ray imaging techniques is limited by the characteristics of the conventional x-ray generator: the wide spectrum which affects dose and contrast, and the relatively large focal spot which introduce blurring and affects the spatial coherence of the beam. As soon as SR facilities were available for research, the community of the medical imaging looked at the x-ray SR beam as an ideal tool. The interest for the radiological applications of SR is based on a number of properties of this radiation and the research in medical imaging with SR may be split in two periods, the first one

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is based on the absorption contrast [2] and the second starts with the advent of the x-ray phase contrast techniques [3].

2. The synchrotron radiation as a quasi-coherent x-ray source for imaging

2.1. Properties of synchrotron radiation

The electromagnetic energy radiated when electrical charges are accelerated, *i.e.* when their trajectory is bent in a magnetic field, is called SR. The most common source of SR is the storage ring that is capable of maintaining charged particles, usually electrons, in a quasi-circular orbit. They circulate within a high-vacuum cavity, which consists of a series of straight sections connected together by bends located between the poles of bending magnets. Under the influence of the magnetic field, the electrons changes direction and an electric dipole radiation is emitted. Due to the relativistic energies of the electrons, the distribution of the emitted radiation is highly peaked in the forward direction and each bending magnet therefore emits a fan of highly collimated SR beam. The wide spectrum depends on electron energy and bending magnet intensity and comprises energies from far infrared up to x-ray. The energy lost by the electrons to this radiation is recovered by the input of radio frequency power and the accelerating radio frequency field forces the electrons to be grouped into bunches, accordingly the radiation has a pulsed structure with a period that is typically a few nanoseconds. Apart from bending magnets as radiation sources in SR facilities, insertion devices may also be placed in the straight section of the ring in order to produce beams with specific properties. It is not within the scope of this paper the discussion of the physics of the SR. A large number of publications are available with different levels of completeness [2,4].

2.2. X-ray imaging with SR

In the field of radiology the ideal beam is tuneable and mono-energetic. This is to avoid beam hardening effect and to allow the patient-based energy optimization according to the large inter-individual variability of humans. The broad and continuous spectrum of the SR is so intense that it is possible to select very tight energy windows to obtain monochromatic x-ray beams suitable for a radiological examination. The monochromator systems, based on perfect crystals (*e.g.* Si) in Bragg or Laue configuration, produce monochromatic beams with high degree of monochromaticy and high flux that are easily tuneable over wide energy range [4]. Another SR property exploited in x-ray imaging is its small source size that is defined by the electron bunches dimension in the vertical direction, and by the collimator aperture at the beamline front-end in the horizontal direction. Moreover due to the natural collimation of the beam, large source to sample distance are applied (up to 100 m) and still being able to effectively use all the produced radiation consequently increasing the spatial coherence of the imaging system.

As a first approximation, a coherent source may be depicted as a mono-energetic and point-like source. The temporal (or longitudinal) coherence describes the energy spectrum and the spatial (or lateral) coherence describes the source size and the geometry of the imaging system. When a coherent source is used for imaging, interference and diffraction effects are observed in simple experimental conditions. For a thorough discussion of the concept of coherence in x-ray see ref [5]. SR beams present a high degree of spatial and temporal coherence. A simple model of the x-ray imaging with a coherent beam is useful for the understanding of the physical foundation of the imaging with SR. Using the wave formalism the plane wave represents a mono-energetic beam traveling in the vacuum given by

$$\psi = \psi_0 e^{\frac{i2\pi z}{\lambda}} e^{-i\omega t} \tag{1}$$

ψ_0 is the wave amplitude, $\frac{2\pi}{\lambda} = |\boldsymbol{k}| = k$ is the modulus of the wave vector parallel to the propagation direction, here the z axis. The last term is the time-dependent factor that will be omitted in the following equations. For simplicity we re-write (1) as follows:

$$\psi = \psi_0 e^{ikz}. \tag{2}$$

If the beam propagates through a homogeneous medium the value of k in (2) changes to $k_{\text{medium}} = nk$.

In x-ray physics, n is usually written as $n = 1 - \delta + i\beta$. δ is the refractive index decrement and β is associated to the decrease of the amplitude. Radiographic images are obtained collecting the x-ray beam that traversed inhomogeneous samples. The properties of the samples are summarized by the refractive index $n(x,y,z) = 1 - \delta(x,y,z) + i\beta(x,y,z)$. The wave emerging from the sample is the result of the product between the incoming radiation and the transmission function, T(x,y), of the object [6] that depends from the refractive index as follows:

$$\psi_{\text{out}} = T(\text{x},\text{y})\psi_0 e^{\text{ikz}} \tag{3}$$

$$T(x,y) = A(x,y)e^{i\phi(x,y)} \tag{4}$$

where

$$A(x,y) = e^{-k\int \beta(x,y,z)dz} \tag{5}$$

$$\phi(x,y) = -k\int \delta(x,y,z)dz. \tag{6}$$

The beam intensity is equal to squared amplitude of the wave thus the linear attenuation coefficient μ (intensity loss per unit path length) is given by

$$\mu(x,y,z) = 2k\beta(x,y,z) = \frac{4\pi}{\lambda}\beta(x,y,z). \tag{7}$$

The physical basis of radiology is the different attenuation of x-rays by different organs of the human body. However, attenuation is not the only effect of the sample on the wave. A phase shift, ϕ, is associated to the refractive index decrement, δ, according to Eq. (6). The phase shift means that the propagation direction of the emerging radiation is modified by the sample, consequently it is no longer a planar wave. The wave vector of the emerging wave, k_{out}, can be written as in Eq. (8), if the spatial derivatives of the wave shift $\phi(x,y)$ are much smaller than the wave number k:

$$k_{out} = \left(\frac{\partial}{\partial x}\phi(x,y)\right)\hat{x} + \left(\frac{\partial}{\partial y}\phi(x,y)\right)\hat{y} + k\hat{z} \equiv \nabla_{xy}\phi(x,y) + k\hat{z} \tag{8}$$

where the xy plane is the object plane. The refraction angle, α, of the beam emerging from the sample at the point (x,y) is

$$\alpha \cong \frac{1}{k}|\nabla_{xy}\varphi(x,y)|. \tag{9}$$

One limitation of radiographs is the small contrast among the soft tissues, *i.e.* between cancer and normal tissues or between blood and cardiac muscle. The administration of contrast agents is a pillar of the modern radiology. The basic idea is to increase the attenuation properties of tissues or organs where the uptake of the contrast agent is higher. The first generation of *in-vivo* SR clinical studies exploited the monochromaticity of the SR beams in presence of a contrast agent [2]. Moreover new x-ray phase-sensitive imaging techniques have been developed in the last two decades to improve the image contrast with the contribution of the phase shift term (Eq. (6)). The application of these techniques in medical imaging is interesting because in the energy range of the soft tissue x-ray imaging (15–25 keV) δ is reported in the range