A HIGH PERFORMANCE DETECTION SYSTEM FOR BREAST TOMOGRAPHY WITH SYNCHROTRON RADIATION

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UN SISTEMA DI RIVELAZIONE AD ALTE PRESTAZIONI PER TOMOGRAFIA AL SENO CON LUCE DI SINCRONTRONE

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Y A LA META ILEGAMOS CANTANDO, O NO ILEGA NINGUNO

“Una perfecta excusa” – Luis Sepulveda and Modena City Ramblers


ABSTRACT

The work performed for the development of detection systems optimized for synchrotron radiation breast imaging will be discussed.

Breast cancer is the most common tumor in the feminine population and, up to now, only surgery and early diagnosis promise a significant mortality reduction. An early detection of the lesions can give a survival expectation higher than 90%.

The SYRMEP (Synchrotron Radiation for MEdical Physics) beamline is operating at the Elettra synchrotron light source in Trieste in the field of medical imaging. The beamline has been modified in order to perform mammographic examinations on patients, which are expected to start next year.

The detection systems described in this thesis are based on a side illuminated silicon microstrip sensor with an application specific read out electronics operated in single photon counting mode. The sensor configuration allows a detection efficiency higher than 80% at all energies of mammographic interest. The visibility of the details in the image is maximized thanks to the single photon counting capability, since the image quality is limited only by the intrinsic fluctuation on the detected photon number.

The FRONTRAD (FRONTier RADiography) detection system has been designed in order to prove the feasibility of clinical synchrotron radiation digital mammography. Silicon sensors with improved efficiency and low leakage current characteristics have been designed and a fast low noise custom integrated circuit has been developed for the application. Prototypes of the detection system have been assembled and tested and the results obtained will be discussed in detail.

Tomographic images of the breast present an enhanced contrast with respect to planar mammography and promise to improve the diagnostic power of the examination, since the breast structures are visible without the overlapping effects present in two dimensional imaging. By using a monochromized synchrotron radiation beam and a high efficiency detector, the dose results comparable to the one delivered in clinical mammography.

The MATISSE (MAmmographic and Tomographic Imaging with Silicon detectors and Synchrotron radiation at Elettra) project is aiming at developing a detector optimized for breast tomography with synchrotron radiation, while upgrading the SYRMEP beamline in order to perform tomographic examinations on patients. The detection system is based on the same sensors developed for the FRONTRAD experiment, commercially available frontend electronics and programmable devices for counting and read out functions. The work concerning the design of the system will be described and the preliminary results obtained with the first prototypes will be presented.
RIASSUNTO

Il lavoro discusso nella presente tesi è stato rivolto allo sviluppo di un sistema di rivelazione per tomografia al seno con luce di sincrotrone su pazienti.

Il cancro al seno è il tumore più diffuso tra la popolazione femminile e al momento la diagnosi precoce e la chirurgia sono le sole metodologie in grado di diminuire significativamente la mortalità. Una rivelazione precoce della presenza di lesioni può dare un’aspettativa di sopravvivenza maggiore del 90%.

La linea di luce SYRMEP (Synchrotron Radiation for MEdical Physics) opera ad Elettra, la sorgente di luce di sincrotrone di Trieste, nell’ambito dell’imaging medicale. La beamline è stata modificata per poter eseguire esami mammografici su pazienti, che dovrebbero iniziare a partire dal prossimo anno.

I sistemi di rivelazione descritti in questo lavoro, sono basati su sensore a microstrip al silicio illuminato lateralmente ed elettronica di lettura operante in modalità di conteggio di fotoni. L’orientazione del sensore permette un’efficienza superiore all’80% nell’intervallo di energie utile in mammografia (17-32 keV). La visibilità dei dettagli nell’immagine è massimizzata grazie alla capacità di contare i singoli fotoni, in quanto la qualità dell’immagine è limitata unicamente dalle intrinseche fluttuazioni Poissoniane del fascio di radiazione.

Il sistema di rivelazione FRONTRAD (FRONTier RADiography) è stato progettato al fine di dimostrare la fattibilità di esami mammografici digitali con luce di sincrotrone su pazienti. Per l’applicazione sono stati sviluppati sensori al silicio di alta efficienza e bassa corrente di buio ed un’elettronica di lettura specifica con caratteristiche di alta velocità e basso rumore. I risultati ottenuti con alcuni prototipi del sistema di rivelazione verranno discussi.

Le immagini tomografiche del seno presentano un accresciuto contrasto e promettono di migliorare la diagnosi in quanto le strutture sono visibili senza le sovrapposizioni presenti nelle immagini bidimensionali. Utilizzando un fascio monocromatizzato di radiazione di sincrotrone ed un rivelatore ad alta efficienza, la dose risulta confrontabile con quella somministrata nella pratica mammografica.

Il progetto MATISSE (MAmmographic and Tomographic Imaging with Silicon detectors and Synchrotron radiation at Elettra) mira a sviluppare un rivelatore ottimizzato per tomografia al seno con luce di sincrotrone e ad implementare il setup tomografico alla beam line SYRMEP. Il sistema di rivelazione è basato sugli stessi sensori sviluppati per l’esperimento FRONTRAD, un’elettronica di frontend commerciale e memorie programmabili per eseguire le operazioni di conteggio e acquisizione dati. Il progetto del sistema di rivelazione verrà descritto e verranno presentati i risultati preliminari ottenuti con i primi prototipi.
## OUTLINE

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INTRODUCTION

The population of industrialized countries enjoys on average a high standard of living. However, together with the increased life expectancy, the incidence of cancer has become more common. With 1 million new cases in the world each year, breast cancer is the most common malignancy in women and comprises 18% of all female cancers [1]. In industrialized countries, breast cancer incidence is increasing, as shown in figure 1, probably due to the life style of women (e.g. more fats in the diet, older age at first pregnancy). However, although surgery is nowadays the only effective way for the cure of the disease, in the last years the mortality is constantly reducing. About 80% of women with breast cancer is cured and the percentage increases to 90% if the tumor is detected in an early stage. The data suggest that the mortality reduction is related to the screening of the population, with consequent possibility of diagnosis of the disease before it induces metastasis in other organs [2].

Nowadays X-ray mammography is considered the most effective tool for the screening of the population. The lesions to be detected are mainly of two kinds: nodules with a size of few millimeters, but absorption coefficient very close to that of the neighboring glandular tissue, and microcalcification as small as a few hundreds microns but with a significant contrast. Although the mammographic examination often allows the detection of the tumor before it becomes palpable, it still has some limitations that result in a high false-positive rate [3]. This problems can be overcome with an improvement of the X-ray source, of the detection system and of the imaging techniques.

The radiation is generally produced by means of X-ray tubes. The photon energies are thus spread over a large spectrum, most of which contributes to the dose of radiation given to the patient, but not to the image quality. This problem can be solved thanks to the use of monochromatic radiation. X-rays produced by a synchrotron light source, besides the possibility of being monochromized thanks to their high intensity, allow one to broaden the capabilities

![Fig. 1: Incidence of and mortality from female breast cancer in England and Wales [4].](image)
of X-ray imaging by means of observing the phase alterations of the wave passing through the sample [5]. In chapter 1 an overview of synchrotron radiation based medical imaging projects will be presented.

The attention will be focused on the activity performed at the SYRMEP (SYnchrotron Radiation for MEdical Physics) beam line at Elettra, the Trieste (Italy) synchrotron light source [6]. The research activities are mainly directed toward the optimization of the mammographic examinations. Given the promising results obtained on test objects and excised tissues, the beamline has been upgraded for performing clinical examinations. In the first phase mammographies will be performed using conventional mammographic screen-film systems, however the perspectives are to move toward digital imaging and then tomographic examinations [7]. The collaboration is thus trying to develop a digital detector optimized for synchrotron radiation mammography.

Digital detectors that could replace commonly used screen-film systems arise great interest in the medical community [8]. The main advantage of the digital approach is the possibility of manipulation by post-processing that can help to enhance the image quality and to apply particular imaging techniques that require data elaboration. In chapter 2 the main parameters for detector evaluation will be presented and some of the digital systems currently used for clinical mammography will be described.

The possibility of using a side-illuminated silicon microstrip sensor with single photon counting readout as digital detector for synchrotron radiation mammography will be discussed in detail in chapter 3.

By orienting the sensor with the strips parallel to the radiation beam (edge on configuration), a high absorption efficiency can be obtained, thus limiting the dose given to the patient [9]. Moreover the photons are converted into electric charge in silicon, without the intermediate step of conversion into visible light in a phosphor, thus avoiding the scattering of light that degrades the spatial resolution of the system.

The high sensitivity of silicon (i.e. large charge produced per photon) allows one to perform the read out with a photon counting technique. A counting system is virtually noiseless, thus the only source of noise is given by the Poisson-like fluctuations of the number of the photons in the beam. The visibility of the details in the image is maximized and the image quality improved at parity of dose [10].

In chapter 4, the FRONTRAD (FRONTier RADiography) detection systems will be described in detail. Silicon microstrip detectors with improved efficiency in the 17-32 keV have been designed and a counting read out integrated circuit able to work at high radiation intensity has been developed [11]. The results obtained with prototypes of such detection system will be presented and discussed. The new ASIC (Application Specific Integrated Circuit) proved a good rate capability. However, some problems have arisen while developing large prototypes, with an increase of noise and disuniformities between the channels. Other solutions for what concerns the readout electronics have thus been investigated.

In particular, the efforts have been directed toward the development of a detection system optimized for breast tomography with synchrotron radiation. Thanks to the absence of superimposition effects, 3D (Three Dimensional) breast imaging promises an improvement of the diagnostic power of mammography [12]. The contrast of the structures is enhanced and the shape of the lesions is detected more clearly. The technique still has some limitations mainly the high dose given to the patients and the poor spatial resolution. However the improvement of computed tomography scanners and reconstruction algorithms is very fast and the perspectives are promising. The use of a monochromatic synchrotron radiation beam allows a significant dose reduction and an enhancement of the spatial resolution [13]. Moreover, the efficiency of edge on sensors is increased at higher energies and counting detectors perform significantly better than integrating ones when few photons per steps have to be detected. In tomography where the energies used
are higher than in mammography, since the breast is uncompressed, and the image statistics is collected over several projections.

The MATISSE (MAmnographic and Tomographic Imaging with Silicon detectors and Synchrotron radiation at Elettra) detection system exploits such solutions and results particularly appropriate for the tomographic application. The system is based on the same sensors as the FRONTRAD experiment, but a different frontend electronics is used in order to overcome the noise problems encountered with the previous system. The readout is based on programmable logic devices and allows thus a completely custom data acquisition [14]. In chapter 5 the detection system will be presented in detail and the results obtained with the first prototypes will be discussed. A 384 channels prototype is now in the testing and optimization phase. The final two layers 20 cm large detector, is to be delivered at the end of 2005 and the future work to achieve this goal will be outlined.
1. SYNCHROTRON RADIATION MAMMOGRAPHY

X-rays were discovered by W. C. Röntgen in November 1895 and the first clinical images were taken already at the beginning of 1896 [15]. The possibility of exploitation of X-rays for medical applications was certainly one of the reasons why Röntgen was awarded with the Nobel prize in 1901 [16].

For almost half a century X-rays were exclusively generated by X-ray tubes, until the SR (Synchrotron Radiation) emitted by charged particle was observed in accelerators built for high energy physics [17]. The optimal characteristics of such radiation suggested the construction of facilities dedicated to this purpose which soon became important centers of X-ray based scientific research. For what concerns the medical field, at the beginning SR was mainly used as golden standard for clinical studies performed in hospitals [18]. However, SR specific medical research began to gain importance and in 1986 the first angiographic examinations on patients were performed at Stanford SSRL (USA). Since then, several medical applications were developed and optimized thanks to the peculiarity of SR.

In this chapter, after describing the properties of SR, the main activities performed at SR facilities in the field of medical research will be highlighted and the attention will be focused on the new clinical mammography facility which is being built in Trieste. The SYRMEP beamline at Elettra updated for in vivo mammographic examinations will be described in detail and the perspectives regarding its activity will be discussed.

1.1 PROPERTIES OF SYNCHROTRON RADIATION

Early synchrotron light sources used photons that were created as the undesirable energy loss of electron accelerators operated for high energy physics research. This parasitic use of synchrotron radiation showed such successful results that in the 80’s accelerators were built expressly for the purpose of generating synchrotron radiation.

A detailed description of SR generation processes can be found in [19].

i. Generation of synchrotron radiation

Electrons are stored in rings where they are kept in a circular orbit. The main components of the storage ring are illustrated in figure 1-1a.

Synchrotron radiation is emitted by bending magnets, or insertion devices i.e. wigglers or undulators that can be inserted in the straight regions.

Next generation synchrotron radiation sources will also include FELs (Free-Electron Lasers).

a. Bending magnets

Bending magnets are present in all circular particle accelerators. The particle passing through a magnetic field is forced to follow a circular trajectory and emits radiation due to the acceleration,
as shown in figure 1-1b.

The radiated power of a charge in a magnetic field can be obtained by the Larmor formula and rapidly increases with the energy of the circulating particle [20]. Since the radiation rate results inversely proportional to the fourth power of the mass of the particle, all SR sources are based on electrons or positrons.

The spectrum of the radiation is continuous and is characterized by a critical energy $E_C$, which divides the spectrum into two parts with equal power [21]. The value of $E_C$ rapidly increases with the energy of the circulating electrons $E$ and is inversely proportional to the curvature of the electron trajectory.

The angular distribution of the radiation is highly peaked in the forward direction. The opening angle for photons of critical energy can be approximated with $\frac{1}{\gamma} = \frac{mc^2}{E}$. The emission cone gets narrower at higher photon energies.

b. Wigglers

Wigglers are insertion devices used in all accelerators specific for SR production. The wiggler is a special magnet with alternating directions of the magnetic field that cause oscillation of the electron bunch, as shown in figure 1-1c. The electron beam wiggles with a large deviation angle. A bright and spectrally continuous light with short wavelengths is obtained.

The photon flux and the radiation intensity are more intense than for the bending magnet of a factor given by the number of poles within the wiggler.

c. Undulators

Undulators are insertion devices where the electron beam wiggles with a small deviation angle, as sketched in figure 1-1d. Sharp energy peaks are obtained due to the coherent interference of radiation emitted at different periods and the photon spectrum is given by harmonic wavelengths proportional to the square of the energy and inversely proportional to the period length. The energy band becomes sharper as the number of periods increases.

The opening angle of the radiation cone is inversely proportional to $\gamma$ and becomes narrower as the number of periods increases.
**d. Free-electron lasers**

FELs are expected to increase the brilliance of SR sources of several orders of magnitude. They will be capable of providing intense, powerful beams of laser light that can be tuned to any precise wavelength [22]. Accelerated electrons pass through a wiggler that causes the electrons to oscillate and emit light which is captured in the cavity, and used to induce new electrons to emit even more light.

**ii. Characteristics of SR**

Figure 1-2 shows the spectral brightness of SR produced by bending magnets and insertion devices with different electron energy. The spectrum and brightness are compared with the ones produced by X-ray tubes. The latter can be taken as a rough estimate since brightness depends strongly on the operation parameters (e.g. kVp, mAs, collimation) and fabrication characteristics of the device (e.g. focus size, stationary or rotating anode).

The principal properties of SR can be summarized as follows [24]:

- High intensity broad and continuous spectrum which makes possible the production of intense tunable highly monochromatic beams. Monochromatization is usually obtained by exploiting Bragg diffraction from crystals [25].
- Natural collimation thanks to the narrow cone of emitted radiation. For example, the horizontal beam divergence at the SYRMEP beamline at Elettra is only 7 mrad [26].
- This property enhances the source intensity, since all the emitted radiation is directed to the sample, and avoids the presence of parallax effects and spatial resolution deterioration in imaging studies.
Medical imaging techniques implemented at synchrotron radiation facilities are mainly based on absorption and refraction of X-rays [5]. Absorption imaging is largely used for clinical radiography based on conventional X-ray tubes, while techniques that exploit phase effects require a high degree of spatial coherence of the radiation and so far their clinical exploitation seems possible only at SR facilities.

In this section the basic principles of both absorption and phase techniques will be discussed. The main applications of SR for in vitro and clinical studies will be highlighted.

i. Absorption imaging

Conventional radiology wants to discriminate the presence of details of different density in the sample by detecting differences in their attenuation coefficients.

a. Principles of absorption imaging

The intensity of radiation passing through a homogeneous sample of thickness $x$ is given by [27]:

$$ I(x) = I_0 e^{-\mu(E)x} $$

(1:1)

where $E$ is the energy and $I_0$ the intensity of the impinging radiation. $\mu$ is the linear attenuation coefficient of the sample:

$$ \mu = (\sigma_{ph}(E) + \sigma_C(E)) \rho $$

(1:2)
which is related to the atomic density $\rho$, and to the photoelectric ($\sigma_{\text{ph}}$) and Compton ($\sigma_C$) cross sections. The pair production cross section can be neglected in the X-ray energy range used in radiology.

The attenuation coefficient is then a function of the sample composition and radiation energy. In the case of polychromatic beams, the attenuation is obtained by integrating over the radiation spectrum.

If we consider a homogeneous sample containing a denser detail as in figure 1-3 we can define the contrast as the relative difference between the transmitted intensities outside ($I_1$) and inside ($I_2$) the shadow of the detail:

$$C = \frac{I_1 - I_2}{I_1} = \frac{I_0 e^{-\mu_1(E)D} - I_0 e^{-\mu_1(E)(D-L) + \mu_2(E)L}}{I_0 e^{-\mu_1(E)D}} = 1 - e^{-\mu_2(E)-\mu_1(E)L}$$

where $\mu_1$ and $\mu_2$ are the attenuation coefficient of the homogeneous background and of the detail respectively while $D$ and $L$ are the sample and the detail thickness respectively.

Given the radiation energy, the contrast is essentially a property of the examined sample and depends on the detail size and on the difference of its attenuation coefficient from the $\mu$ of the background.

However, the visibility of a detail depends not only from its contrast but also from the image quality, which is affected by the beam quantum mottle (i.e. the Poisson-like fluctuations on the incident number of photons) and possibly by the noise of the detection system [28].

The SNR (Signal to Noise Ratio) of the detail $\text{SNR}_{\text{detail}}$ can be defined as:

$$\text{SNR}_{\text{detail}} = \frac{|I_1 - I_2|}{\sqrt{\sigma_1^2 + \sigma_2^2}}$$

where $\sigma_1$, $\sigma_2$ is the standard deviation outside and inside the shadow of the detail. In an ideal imaging system the fluctuation on the number of photons is purely Poisson-like thus $\sigma_1 = \sqrt{I_1}$ and $\sigma_2 = \sqrt{I_2}$.

$\text{SNR}_{\text{detail}}$ generally increases with the number of detected photons.

The dose $D$ given to the patient is defined as the energy deposited per mass unit. It depends on the energy of the radiation (being related to the absorption of radiation and consequently $\mu$) and on its intensity. Although the calculation of the dose is usually very difficult and time-consuming, it is possible to demonstrate that the FOM (Figure Of Merit): 

$$\text{FOM} = \frac{\text{SNR}_{\text{detail}}}{\sqrt{D}}$$

is a function of the beam spectrum, of the sample characteristics and of the detection system features. The FOM is independent from the radiation intensity and can thus be used in order to optimize the image quality independently from the dose given to the patient.

**b. Advantages of synchrotron radiation**

SR offers several advantages for absorption contrast imaging [18]:

- The use of monochromatic beams allows the optimization of the energy as a function of the radiographed sample in order to maximize the FOM. Moreover the hardening of the beam due to the sample absorption of the low energy photons is avoided, contributing to limit the dose.
  - This feature can be also exploited in order to apply KES (K-Edge Subtraction) [29]. In this case, images are acquired at energies above and below the K-edge of the contrast agent used.
and then the two images are subtracted.

- The small source size, the negligible divergence and the large distance of the sample from the source allow a good spatial resolution, which is limited only by the detector.
- The laminarity of the beam due to the small opening angle in the vertical direction and the possibility to place the detector at a large distance limit the presence of scattered radiation in the images. However scanning is required for 2D (Two Dimensional) imaging.

c. Applications

Some applications of SR medical imaging with past experience or perspectives for in vivo studies will be described [18].

- **Coronary angiography**
  Clinical coronary angiography is an important diagnostic method, which provides detailed high-resolution images of the coronary arteries. It is largely used for follow-up of patients who have undergone an angioplasty surgery in order to detect in-stent restenosis. However, in clinical practice complications and mortality are too frequent since the contrast agent must contain a high concentration of iodine and must be injected directly into the artery.
  When using SR, a much lower concentration of contrast agent can be used and it can be somministrated by intravenous injection [30, 31, 32].
  Coronary angiography is the only medical application for which synchrotron radiation techniques have been extensively applied in human research. So far, a total of 500 patients have been imaged in several SR facilities.
  The experimental setup is implemented by means of a bent Laue monochromator. The radiation has a vertical energy gradient and two beams of energy above and below the K-edge are obtained by means of a splitter that absorbs the intermediate energies. The two beams are focused in correspondence of the patient, who is scanned through the beam, and then detected by two different sensors.

- **Bronchography**
  Bronchography can be used for the detection of lung cancer or for the diagnosis of respiratory diseases.
  In lung imaging with SR, xenon mixed with oxygen is used as a contrast agent. The bronchial tree is clearly visible after a few inspirations, but is then shadowed by the filled alveoli.
  So far there has been only one human study that demonstrated that the bronchial tree could be imaged down to the fourth bifurcation [33].
  SR bronchography suffers the concurrence of other techniques such as computed tomography who has dramatically improved in the last years. However KES bronchography maps the ventilation in lungs with good spatial and temporal resolution and is expected to contribute to the study on lung diseases and on the effect of drugs. Small animal studies for quantitative analysis of lung ventilation and diseases show interesting perspectives [34].

- **Mammography**
  Mammography is the most effective technique for early diagnosis of breast cancer. In conventional mammography radiation from a fine-focus molybdenum anode X-ray tube is generally employed, thus at SR facilities X-rays in the 15-22 keV energy range are used.
  SR mammography studies are carried on in order to develop new methodologies to import into the clinical standard. Experimentations on humans are forseen only in order to discriminate sick patients from false-positives in case they have undertaken an ambiguous mammogram, before they have to undergo a biopsy, as will be discussed in section 1.3.
  Compared to conventional mammographic units, SR mammography shows a great
improvement of the image quality-dose relationship, which is due to the beam monochromaticity and to the high collimation of the beam, which strongly removes the presence of scattered radiation in the images using a slit instead of anti-scattering grids [35, 36]. Dual energy mammography is being studied in order to remove the contrast due to the distribution of the glandular tissue and enhance the intrinsic contrast of pathological tissues [37]. Recent developments in phase contrast imaging are greatly improving mammographic studies, as will be described in the next paragraph.

**ii. Phase detection imaging**

Thanks to the high spatial coherence of SR, in recent years imaging techniques based on phase effects have been largely investigated [38].

**a. Principles of Phase detection**

The contrast can be achieved by exploiting refraction differences in samples that normally show no or little absorption contrast.

The refraction index $n$ is composed by an imaginary component $\beta$ related to the absorption and by a real component $\delta$ which defines the diffraction of the waves [39]:

$$n = 1 - \delta + i\beta \quad (1:6)$$

In the energy range suitable for X-ray imaging of biological samples, $\delta$ can be considerably larger than $\beta$.

Phase techniques are sensitive to the gradient of the refraction index, thus strong edge enhancement effects are visible at the borders of details. The refraction pattern is characterized by positive and negative peaks near the borders. The contrast must then be redefined:

$$C = \frac{I_1 - I_2}{I_0} \quad (1:7)$$

where $I_1, I_2$ are the intensities on the maximum and on the minimum respectively, while $I_0$ is the intensity in the background.

It is interesting to point out that the mechanism that gives rise to phase contrast deposits no dose in the sample [40]. It is of course impossible to eliminate the processes that produce the absorption of radiation, but it may be possible to operate in conditions where those are minimized. The real part $\delta$ of the refractive index decreases an order of magnitude less than the imaginary part $\beta$ for energies that go from 20 keV to 60 keV. By increasing the energy, phase contrast imaging could allow a significant dose reduction with little deterioration of the image quality. However, more work is needed in order to determine if the loss in absorption contrast that would result in using higher energy X-rays could be replaced by the information given by phase contrast.

Phase shift effects can be detected mainly with two different experimental setup i.e. in-line phase contrast and DEI (Diffraction Enhanced Imaging).

**b. In-line phase contrast imaging**

In-line phase contrast is obtained with the same setup of absorption imaging, only by increasing the distance between sample and detector, and does not require any kind of image reconstruction or wave splitting [39, 41].

Figure 1-4 schematically shows the process that governs phase contrast imaging. The
interference between elastically scattered waves and the unrefracted waves is detected. The radiation is elastically scattered at very small angles (\(\sim 10^{-100} \mu\text{rad}\)) [42]. The contrast is proportional to the second derivative of the electron density of the sample, so that interfaces and boundaries are enhanced in the images. The interference pattern results in in narrow peaks and valleys along the borders of the details, strongly enhancing the visibility of thin and tiny details that would normally be invisible in absorption based images.

Since the detector has a finite resolution, the distance between the sample and the detector must be of several meters in order to detect phase effects. The interference pattern must be convolved with the detector response, resulting in a loss of signal for detectors with a poor spatial resolution. The interference pattern must also be convolved with the source shape. The distance must consequently be optimized as a function of the detector resolution and source size. The beam must be transversely coherent over the detail being imaged, but the longitudinal coherence is not fundamental, so that even polychromatic radiation can be used [43].

An appropriate high efficiency detection system can prove the feasibility of phase contrast imaging increasing only slightly the dose with respect to SR absorption imaging [39].

Phase contrast detection can be enhanced by partially illuminating the sensor as described in [44, 45].

c. Diffraction enhanced imaging

With diffraction imaging, only the photons scattered by the sample at a certain angle are detected [39]. This is usually achieved by using an analyzer crystal between the sample and the detector. The analyzer is aligned in order to select only the photons refracted to a certain angle by Bragg diffraction. If the analyzer crystal is aligned with the monochromator, the scattered X-rays will be rejected, while with a slight misalignment only the scattered radiation will be detected. The scattering angle selection by means of Bragg diffraction can be achieved only with monochromatic radiation, however SR is not necessary and monochromized radiation from an X-ray tube has also been used [46].

The diffraction angle is, to the first approximation, proportional to the gradient of the phase-shift term \(\delta\), so the border visibility will be enhanced. By acquiring images with opposite
misalignments of the analyzer crystal and combining the two, images that carry pure absorption and diffraction information can be obtained.

A different setup can be obtained by positioning a linear detector slightly out of the beam \([44, 45]\). By tuning the detector displacement with respect to the beam and the sample to detector distance, the diffraction angle and acceptance window can be selected. With a sample to detector distance of about 2 m and a displacement of 15-20 \(\mu m\), the scattering angle detected is a few tenths of microradians. In this setup, the large dimensions of the pixel are not a disadvantage up to a certain limit, since the acceptance window, and thus the signal in the image, increases. Since the photons are deviated by a very small angle a negligible parallax effect is present and the shape of the details is preserved in the image. Although the resulting scattered radiation has a low intensity, a high \(\text{SNR}_{\text{detail}}\) can be obtained, since the contrast is very high. It is important to notice that with this setup the detection of scattered radiation can be achieved at no dose expenses simply by adding a further line of pixels just above or below the detector layer used for conventional absorption or phase contrast imaging.

d. Applications

Phase contrast methods strongly enhance the differences between soft biological tissues of very similar absorption strengths and thus find application in very challenging diagnostic examinations. Phase contrast techniques, though, have yet to be applied to patients and hence the current “state of the art” is restricted to small animals and human tissue samples \([40]\).

- **Cartilage and bone imaging**
  The imaging of cartilage and bone is important for the development of successful treatments for conditions such as degenerative osteoarthritis and joint diseases. There is considerable interest in using phase contrast to detect early degenerative changes of cartilage. Phase contrast proved to clearly delineate the interface between air and soft tissue and between soft tissue and cartilage \([47]\). Moreover DEI provides distinction between degenerated and healthy cartilages \([48]\).

- **Lung imaging**
  The large refractive index of air and soft tissues makes the lungs an ideal candidate for phase contrast imaging. Works in this area are at a very early stage but early comparative studies on small animals and human tissues have been conducted \([49, 50]\).

- **Mammography**
  The poor contrast due to small X-ray absorption differences is particularly relevant in the field of mammography, where low contrast masses and small size calcifications have to be detected. For this reason phase contrast techniques have been largely applied to the mammographic field and a number of researchers have imaged breast tissues using in-line phase contrast and diffraction enhanced imaging. In-line phase contrast provides enhanced contrast and spatial resolution with better definition of the glandular component and improved visibility of micro-calcification \([39]\). DEI proved an enhanced visualization of lesion spiculation and architectural distortion and in particular lobular carcinoma, which is a difficult tumor to detect, was better diagnosed \([51, 52]\). DEI mammography has been investigated also with a conventional source and an analyzer crystal \([46]\). The mammographic application is the one which shows better perspectives both with conventional sources \([53, 54]\) and synchrotron radiation. The possibility of exploitation of in-line phase contrast imaging is certainly one of the motivation for the construction of the beamline for clinical mammography which is being built at Elettra in Trieste and will be...
a) First floor

b) Second floor

Fig. 1-5: Overview of the SYRMEP hutch. a) On the first floor are located the mammographic station, the radiologist room, the experimental room and the beam preparation facilities. b) On the second floor is positioned the control room.

described in the next section.

1.3 SYRMEP

The SYRMEP beam line has been active in the field of medical imaging since 1996 at Elettra, the Trieste (Italy) SR facility [6].

Taking into account the typical energy spectrum at a bending magnet at Elettra (which operates at 2 and 2.4 GeV) and considering the very high social relevance of the breast cancer incidence in the female population in Europe, the local medical community indicated that mammography was the most suited medical application for the beamline.

The results on the feasibility studies on conventional and phase contrast imaging on test objects and human breast tissue samples have been considered very successful by the community of radiologists [39].

The following phase of the study involves the clinical validation of the technique on a limited number of patients selected by radiologists according to a predetermined recruitment protocol. In this context, an agreement among the Public Hospital, the University and Elettra in Trieste, have been established in order to implement a medical facility dedicated to mammography. The previous layout of the beamline has been deeply modified in order to perform in vivo mammographic examinations.

In order to allow enough room for the mammographic station, the spaces have been distributed on two floors, as shown in figure 1-5. On the first are located the rooms for the radiologist and the patient, which are separated by a lead-glass window. On the second floor is located the beamline control room. Ahead of the mammographic station, on the first floor, a room for performing the standard experimental activity has been preserved.

In this section the layout of the beam line and of the new mammographic station will be described in detail and an overview of the perspectives for its operation will be pointed out.
i. The beamline

Figure 1-6 shows the main components of the SYRMEP beamline. The first element after the frontend is a 2 mm beryllium window which divides the ultra-high vacuum of the ring from the beamline and eliminates the low frequency components of the radiation. A system of slits allows to select the beam size and shape with a micrometric precision. The monochromator allows the selection of the energy in the 8-35 keV range with 0.2 % precision. It consists of two parallel silicon crystals cut in $\langle 111 \rangle$ orientation. The energy selection is obtained by Bragg diffraction tilting the crystals. The second crystal can also be translated in order to maintain the same beam position at all energies.

A second 0.5 mm beryllium window separates the vacuum components of the beamline from the rest of the setup. The measured photon flux after this second window is plotted in figure 1-7. The radiation intensity can be attenuated thanks to a system of aluminum filters of thickness ranging between 250 $\mu$m and 8 mm. A second system of slits is used to shape the beam and stop the radiation scattered by the previous elements of the beamline. The maximum beam cross section is $210 \times 4 \text{ mm}^2$ in the patient room.

The beam then enters the experimental room. A system of motors for sample and detector movement and positioning is located on two optical tables. For the acquisition of planar images...
the sample is scanned through the beam, while for tomographic imaging it is rotated in discrete steps. If a SF (Screen-Film) system is used as detecting medium, it will also be scanned in front of the beam. The film scanning speed is determined by the dose requirements for a correct film exposure (see section 2.1), while the sample scanning speed is chosen in order to preserve the angular velocity with respect to the source avoiding artifacts.

Before entering the patient room a system of two identical ionization chambers measures the intensity of the radiation and fast and safety shutters are used for the control of the exposition during the examination.

\[ \text{ii. The mammographic station} \]

The main upgrades of the beamline for the clinical examinations consist in the implementation of the patient and detector movement and positioning system and of the safety and control systems [7, 55].

\[ \text{a. The patient support} \]

An innovative remotely-controlled support has been developed for the positioning and movement of the patient [7, 55]. It consists in a bed with a hole, as shown in figure 1-8 and is designed and realized by CINEL (Italy) in collaboration with IMS, an Italian producer of standard mammographic units. The patient will be positioned prone with the breast dangling and the examination will be performed by scanning the organ through the beam. The patient support is equipped with three motion stages: horizontal, for patient positioning, vertical, for positioning and scanning of the organ, and rotational along an axis orthogonal to the beam, in order to acquire images with different projections and perform tomographic examinations. The scan velocity can be accurately selected up to 4 cm/s.

The breast compression paddles are located under the hole in the support: they are motorized and one can also be positioned manually for fast release.

The detector holder is designed in order to contain a mammographic screen-film cassette, as shown in figure 1-9a. It is placed on a 2 m long linear guide in order to select the optimal organ-to-detector distance for phase contrast examinations, and is moved vertically simultaneously with the patient support. Absorption and in-line phase contrast images can be acquired, while the setup

Fig. 1-8: Pictures of the patient support. In the second picture the detector holder, the rail for its positioning, the breast compressor and the motors group are also visible.
for DEI examinations has been considered too challenging for clinical examinations and has not been implemented because of the strict requirements on the alignment of the analyzer crystal. Instead of the antiscattering grid used in conventional mammography, the system has a slit aligned with the beam in front of the detector holder: only the primary and very small angle scattered beam will impinge on the SF cassette.

A laser based system for locating the position of the beam on the breast has been implemented.

b. Safety, dosimetry and control systems

The radiation monitors are an upgraded version of the ionization chambers working at the DESY beamline, calibrated under compliance with ENEA, the Italian metrology institute for ionizing radiation [7,55]. The picture of one of the chambers is shown in figure 1-9c. The beam is parallel to the electric field and the entrance and exit Al-mylar windows are the electrodes. The uniformity of the ionization chambers response has been investigated by measuring the signal output due to a pencil beam moving on the entrance window and parallel to the electric field. The maximum observed difference in response is about 1%. The stability in time has been evaluated in the ENEA laboratories and is compatible with the required national standard stability.

The parameters of the examination will be selected by evaluating the organ characteristics thanks to an exposimeter. It consists of a photodiode located in the detector holder (as shown in figure 1-9b) that will be flashed with radiation before performing the examination. The thickness of the breast is provided by the compressor and it will be possible to calculate the glandularity of the organ (i.e. the fraction of glandular tissue with respect to fat tissue) by comparing the signal of the ionization chambers placed before the organ with that provided by the exposimeter. This data
are then used for the selection of the X-ray energy and of the scanning speed of the examination in order to maximize the FOM and obtain the correct exposition of the film [56].

An automated system will control the patient movement and provide the opening and closing of the shutters. The safety system will stop the examinations whenever an emergency is encountered, the patient movement is compromised or the dosimetry system reads out anomalous data. The time for processing the data and closing the shutters is of only a few tens of milliseconds. The project for the fast and safety shutters has been developed in collaboration with the groups of DESY and ESRF medical beamlines. The systems have been designed in order to be redundant and fail-safe in order to guarantee complete safety to the patient.

Since there are no previous cases of SR mammography, the development of a protocol for the selection of examination parameters and for the quality control of the entire setup is being carried on [56].

1.4 OUTFLOOK

A monochromatic synchrotron radiation beam is an optimum instrument for X-ray imaging. The peculiar characteristics of synchrotron radiation allow not only to enhance the quality of radiographic images, but also to apply innovative techniques in order to observe the phase alterations of the radiation transversing a sample.

Synchrotron radiation finds application in many medical tasks. For what concerns mammography, it allows a high resolution detection of low contrast lesions with low doses given to the patient.

The mammographic facility at the SYRMEP beamline is under commissioning and has recently been approved by the local Ethical committee, but still needs to be approved by several institutions and in particular by the Italian Health Ministry [7, 55]. At an early stage of the clinical studies, only doubtful cases will be examined: women who have undertaken a conventional mammography with an ambiguous diagnosis will be offered the possibility of undergoing a SR mammography before executing a biopsy. A set of absorption and phase contrast mammograms on a statistically significant number of patients will be acquired. The goal is to perform a comprehensive study on advantages and limitations of clinical SR mammography in comparison with conventional mammography.

The next step will be the integration in the mammographic station of the digital detection system that will be described in the next chapters. Digital mammography will be the first stage of the examination while a few tomographic slices will be acquired in order to investigate doubtful structures. The advantages of breast tomography will be discussed in chapter 5.

Long time perspectives, involving clinical research, technology transfer and clinical practice, may arise from the outcome of this research. In case of successful results, a fully mammographic beamline could be implemented in order to carry out a large number of clinical examinations exploiting other promising and innovative techniques (e.g. dual energy imaging, diffraction enhanced imaging). Moreover, a still greater interest may arise in upgrading clinical mammographic units in order to provide characteristics similar to SR facilities (e.g. quasi-monochromatic sources, laser plasma based sources, breast tomography units).
2. DIGITAL MAMMOGRAPHY

Since the mid ‘90s there has been a great interest in DM (Digital Mammography), but the shift from SF to digital detections systems has been slowed down by technical challenges and high costs due to very strict demands in terms of high image quality and low absorbed dose in mammography [57].

Mammography with SF technique, in fact, is fast and cost efficient, providing high sensitivity and specificity [29, 58]. On the other hand, a major feature of DM is that the processes of image acquisition, image display and image storage and retrieval are decoupled, allowing each to be optimized individually [8].

A digital image is built up as a matrix of pixels whose content represents the average of signal acquired by the corresponding detector element.

The main advantage of the digital approach is the possibility of image manipulation by post processing. This can be used simply in order to enhance particular image features or for the application of special imaging techniques, like dual-energy mammography [59, 60, 61], contrast subtraction mammography [62, 63] or computed tomography [12, 52, 64, 65]. This last application will be reviewed in detail in chapter 5.

A digital image is also characterized by ease of storage and retrieval and can be transmitted for remote diagnosis (telemedicine) or processed by computer aided diagnosis software in order to enhance the accuracy of interpretation [66, 67].

Since the performances of the detector play a key role in the image quality obtained, general considerations about the detector evaluation will be pointed out, with a particular emphasis on the features that are exploited by the detection systems developed in this work. Moreover a brief review of existing DM systems will be presented.

2.1 DETECTOR EVALUATION

The characteristics of the detector are very important in determining the efficiency with which the images are produced and their intrinsic quality.

The quality of an image is closely correlated with its diagnostic value, but can slightly differ from it [66]. Since the optimization of the diagnostic effectiveness of the image is the main goal of medical imaging, the best way of comparing the performance of different detectors is to study the sensitivity and specificity of the diagnosis obtained with the different detection systems.

Some of the most important features of detector performance are efficiency, spatial resolution, geometrical characteristics and field coverage, dynamic range and uniformity. These features are correlated to each other and different technologies need compromises among these factors.

i. Efficiency

The efficiency of a detector is of fundamental importance in order to limit the dose given to the patient. The possibility of exploiting the information given by the radiation impinging on the detector is mainly determined by two terms: the efficiency, i.e. the probability of absorption of the radiation inside the detector, and the signal collection efficiency.
The absorption efficiency $\eta$ of the detector for photons of energy $E$ is given by:

$$\eta(E) = 1 - e^{-\mu(E)T} \quad (2:1)$$

where $\mu$ is the linear attenuation coefficient of the sensor and $T$ is its thickness. For polyenergetic sources (e.g. X-ray tubes) the effective efficiency of a detector will be obtained by integrating $\eta$ over the radiation spectrum. If the detector is shielded by its packaging, by a layer of protecting material or by an insensitive region in the entrance window of the detector, the efficiency will be lower:

$$\eta(E) = (1 - e^{-\mu(E)T})e^{-\mu_s(E)T_s} \quad (2:2)$$

where $\mu_s$ is the attenuation coefficient of the shielding material and $T_s$ is its thickness.

The quantum interaction efficiency can be maximized by increasing the detector thickness or using materials with high atomic number, while reducing the thickness and density of the shield. $\eta$ depends strongly on the energy of the impinging radiation, which influences both the detector and the shield absorption.

The efficiency $\eta$ depends only on the absorption due to the detector and not on its performances. It is possible to define the DQE (Detected Quantum Efficiency) of the detection system as the squared ratio between the SNR of the signal at the output of the detector ($\text{SNR}_{\text{out}}$) and the maximum possible SNR, which corresponds to the one at the input of the detector ($\text{SNR}_{\text{in}}$):

$$DQE = \frac{\text{SNR}_{\text{out}}^2}{\text{SNR}_{\text{in}}^2} \quad (2:3)$$

In an ideal system, the signal fluctuations at the input of the detector are due only to the Poisson-like fluctuations ($\text{SNR}_{\text{in}} = \sqrt{N}$) of the beam (quantum mottle), which propagate to the output due to the finite absorption of the detector ($\text{SNR}_{\text{out}} = \sqrt{\eta N}$). In this case the DQE results exactly equal to the efficiency. However it is not uncommon that the detector adds some noise to the signal, so that the DQE results lower than $\eta$.

**ii. Spatial resolution**

Most detectors for digital radiography are composed of DELs (Detector ELEments), usually of constant size and shape. The PSF (Point Spread Function) is the image of an ideal point-like object and is often used to assess the spatial resolution of an imaging system. It will be at least one pixel wide (as shown in figure 2-1a), but can also consist of a spot of several pixels, brighter in the center and progressively darker away from the center. The resolution can be defined as the width within which the PSF drops to half the maximum value, called FWHM (Full Width at Half Maximum). The PSF does not need to be symmetrical, so there may be different spatial resolutions in different directions. If the object consists of two ideal points, just a distance FWHM apart, they can be considered separated in the image.

The MTF (Modulation Transfer Function) is formally defined as the magnitude of the Fourier transformed PSF. The physical meaning of the MTF is to evaluate the fraction of the contrast at a specific resolution that is transferred by the imaging process. In the optimal case, the MTF value is 1, meaning that object and image contrasts are identical. The MTF is computed in the Fourier domain and is thus expressed in spatial frequency units. The MTF usually starts with a value 1 at 0 spatial frequency which represents a homogeneous background. It then drops down to zero in a system-specific manner. The MTF of a detector with a rectangular pixel is shown in figure 2-1b.
The spatial resolution of two systems can readily be compared by using the MTF: at each spatial frequency the system with the higher MTF maintains a better contrast. The dimension of the active portion of each DEL defines an aperture $d$ which determines the spatial frequency response of the detector, as shown in figure 2-2.

The sampling interval $p$ of the detector is the pitch between sensitive elements of measurements. The FF (Fill Factor) provides a measure of the detector’s geometric efficiency and is given by:

$$ FF = \frac{d_x d_y}{p_x p_y} \quad (2:4) $$

considering that $d$ and $p$ can be different along the two coordinates of the image.

Some detectors are not pixellated at the X-ray absorption stage (e.g. photostimulable phosphor detection systems), but the aperture dimension and sampling interval are defined by the read out mechanism.

The sampling theorem states that only spatial frequencies below $(2p)^{-1}$ (the so called Nyquist frequency) can be faithfully imaged. If the pattern contains higher frequency components, aliasing...
occurs. In this case the frequency spectrum of the image pattern beyond the Nyquist frequency is folded around that frequency.

The smallest sampling interval in a single image acquisition is $p=d$. A method for increasing the Nyquist frequency is 

**dithering**, which consists in acquiring the image several times with a motion of the detector by a fraction of the pixel pitch. This technique is particularly useful when operating scanning detection systems.

### iii. Geometrical characteristics

The imaging system must be able to record the transmitted X-ray signal over the projected area of the organ under investigation.

For example a standard mammographic cassette has a dimension of $18 \times 24$ or $24 \times 30 \text{ cm}^2$, which can give an estimate of the required area to be covered in breast imaging.

There are two main geometrical approaches: one is to develop full field detectors, the other is to use smaller detectors and scan them, together with a collimation slit, as shown in figure 2-3. The main advantages and disadvantages of the two system types will be presented in section 2.3.

Full field detectors can be further divided in two general types: replaceable cassettes or captive sensors. The first type has the main advantage of being compatible with most mammographic stations, although it adds to the acquisition the processes of loading, unloading and specific cassette read out.

On the other hand a captive receptor, which is permanently mounted on the mammographic station, allows a more simple protocol, but requires higher costs because of the need of designing a custom mammographic equipment with integrated detection system. Scanning systems are always captive sensors.

All the geometrical approaches should not impair access to the interesting diagnostic regions (e.g. in mammography the patient’s chest wall) and should minimize the dead regions. This issue is particularly challenging when several detector modules are tiled in order to cover a wider field of view.

### iv. Dynamic range and sensitivity

One of the main limitations of SF systems is their response curve to X-ray exposure. Figure 2-4 shows the relation that exists between the exposure and the optical density obtained for a film after development. For exposures in the toe or in the shoulder region, no detail is visible. The linear region is usually kept narrow in order to enhance the image contrast, but mistakes in exposure
time selection may lead to the need of repeating the examination. The use of a digital system can overcome this problem.

The DR (Dynamic Range) of a digital system can be defined as:

$$DR = \frac{X_{\text{max}}}{X_{\text{noise}}}$$  \hspace{1cm} (2:5)

where $X_{\text{max}}$ is the X-ray fluence providing the maximum signal that the detector can accommodate, while $X_{\text{noise}}$ is the fluence that provides a signal equal to the quadratic sum of the detector and X-ray quantum noise.

The higher the dynamic range, the wider the linear region of the detector response. In mammography the DR is usually requested to be higher than $2^{10}$.

In the definition of DR, the maximum exposure supported by the detector and the minimum detectable signal assume great importance. Since the final output of all detectors is an electrical signal, the sensitivity of a detector can be defined in terms of the charge produced in the detector per X-ray quantum of specified energy. This is strictly dependent on the conversion efficiency of the specific detector, which can be expressed in terms of the energy required to release a light photon in a phosphor (e.g. 13 eV in GdSO$_2$) or to create an e-h (electron-hole pair) in a semiconductor (e.g. 3.6 eV in high-purity silicon) or a photo-conductor (e.g. 50 eV in amorphous selenium) or an electron-ion pair in a gaseous detector (e.g. about 30 eV). The higher the sensitivity, the lower is $X_{\text{noise}}$ at parity of electronic noise.

v. Uniformity

It is important that a radiographic imaging system provides uniformity, i.e. constant sensitivity over the entire area of the image. Patterns that could arise from disuniformities may in fact affect the diagnostic value of the image.

From the definition of $\text{SNR}_{\text{detail}}$ in equation 1:4, one can see that an increase of the disuniformities between pixels (and thus an increase of $\sigma_1, \sigma_2$) leads to a loss in the visibility of the detail. In a digital system the difference in response from element to element can be partially corrected with a calibration of the detector. This is usually accomplished by imaging an object of uniform X-ray transmission, recording the detector response and using it it as a correction mask (flat field). If the detector response is linear, also a mask obtained without radiation (dark field),
to be subtracted to both the image and the flat field before the correction, can be requested. If the response is not linear, flat fields at various photon fluences must be collected.

Moreover, the detector performances should be monitored in order to maintain the response constant over time.

2.2 X-RAY CONVERSION

The basis of most medical X-ray imaging systems is a phosphor layer or scintillating screen. These systems are often used in order to achieve a higher efficiency, but have also some disadvantages. The light quanta produced in the screen must be transmitted to the electronic sensor, which must be correctly coupled in order to achieve an efficient signal collection. During the diffusion the light suffers multiple scattering by the phosphor grains before it escapes the screen, as shown in figure 2-5a. The scattering causes image blur and resolution loss. The screen choice is a trade-off between X-ray absorption and blurring, since thick phosphor screens provide a higher efficiency but cause more light spread.

The blurring problem has partially been solved by developing custom geometries for the coupling between phosphor and detector or through the use of structured scintillating screens. The latter are usually fabricated using columnarily grown CsI; the cracks between the columns refract the light, thus limiting the spread, as shown in figure 2-5b. However, the FWHM of the light spread is generally 1.5 times the thickness for a non-structured phosphor and not much smaller than the scintillator thickness for columnar CsI.

Detectors avoiding the light conversion stage (figure 2-5c) have also been developed. The e-h (or electron-ion) pairs are driven to the collection region by a strong electric field, thus limiting the charge diffusion and solving the blurring problem.

The materials used used for direct conversion are photo-conductors, semiconductors or gases. A good efficiency is maintained thanks to the use of high atomic number materials (mainly selenium [68, 69, 70], but possibly also GaAs [71, 72, 73], CdZnTe [74, 75], InP [76, 77], HgI [78]) or of particular geometrical configuration [6, 79, 80] in order to increase the sensitive absorbing length, as will be presented in section 3.2.

Another important advantage of direct conversion detectors is that the sensitivity is usually much higher than that of phosphor screens (particularly in semiconductor materials), so that the collected charge per X-ray quantum is higher. This allows single photon counting read out, with the advantages that will be presented in section 2.4.

2.3 FIELD COVERAGE APPROACHES

While the main advantage of full field systems is to acquire the whole mammographic image in one single shot, scanning systems are a way of overcoming the size and costs limitations of
available high resolution photo-detectors: the sensor is essentially 1D (One Dimensional), while the second dimension is acquired by scanning detector and X-ray beam across the patient.

The main advantages of scanning systems are not only the reduced costs of the materials of the detector but also the improvement of scattering rejection. Since anti-scattering grids can be avoided, there is an increase of the efficiency of the detector without degradation of the image quality.

The main disadvantage of the scanning approach is the longer duration of the clinical examinations, that can be up to several seconds. This leads to two main consequences:

- Overheating of the X-ray tube, since most of the X-ray flux is removed by the collimators and its exploitation is inefficient. This problem can be partially solved only by the use of X-ray tubes with special cooling or of X-ray focusing systems [81, 82].
- Unease for the patient, who must have the organ compressed for a longer time. However the scanning does not present additional problems of motion artifacts and can possibly reduce the blurring since the acquisition for each position lasts for a shorter time.

The use of multi-line detectors can strongly reduce the acquisition time.

2.4 READ OUT TECHNIQUES

X-ray detection can be handled mainly in two ways:

- Integration i.e. the radiation intensity is measured over a frame period by recording the level of a quantity that typically changes as energy is deposited;
- Photon counting i.e. single X-ray quanta are detected as they reach the detector by comparing the signal with a threshold level, and are then counted on a given time slot.

The main advantage of integrating devices is that they can support very high input fluxes [83]. However, their noise is usually higher than that of counting systems and depends not only on the Poisson-like distribution on the number of absorbed photons \( N = \eta N_0 \), but also on the average charge created per X-ray \( g \), which is different for photons of different energy introducing further fluctuations and attributing different weights to X-rays. In particular the weight is higher for higher energy photons, though their contribution to the contrast is smaller. The number of electrons \( n_e \) collected by an integrating device in a given time slot is:

\[
n_e = \eta N_0 g
\]

where \( N \) is the number of photons impinging on the detector. Stochastic amplification of photon noise by one stage of an imaging system is shown to constitute an effective signal to the next stage, while the underlying photon-noise component is unaffected by a subsequent scattering process [84]. The fluctuation on the detected charge results:

\[
\sigma_e^2 = n_e g \left( 1 + \frac{\sigma_x^2}{g^2} \right)
\]

and considering that both the number of photons and the charge produced per photon are Poisson distributed we have:

\[
\sigma_e = \sqrt{(g+1)n_e}
\]

Moreover, all integrating detectors exhibit also dark noise (reset noise \( \sigma_r \)) and possibly read out noise. These are often related to temperature and cooling can help, however these noise sources set a limit on the sensitivity of the detector. Modern detectors present an electronic noise that can be of the order (or smaller) than the charge created by a single photon:

\[
\sigma = \sqrt{(g+1)n_e + \sigma_r^2}
\]
The SNR at the output of the detector ($SNR_{out}$) results:

$$SNR_{out} = \frac{n_e}{\sqrt{(g+1)n_e + \sigma_r^2}} = \frac{\eta N_0 g}{\sqrt{(g+1)\eta N_0 g + \sigma_r^2}}$$

(2:10)

and is plotted in figure 2-6 compared to the purely Poisson-like $SNR_{out} = \sqrt{\eta SNR_{in}}$ of a noise free counting system.

The DQE of an integrating system results always lower than the one of a counting system (equation 2:3):

$$DQE_{integration} = \frac{g}{(g+1) + \frac{\sigma_r^2}{\sqrt{\eta N_0 g}}} DQE_{counting} < DQE_{counting}$$

(2:11)

The difference is particularly significant when less then 1000 photons are detected, as can be in low dose applications, scanning systems or computed tomography where the statistics on the image step is low.

Integrating devices can also saturate due to the accumulation of a high quantity of energy. This sets a limit on the flux that can be integrated before the detector is read out and the pixel reset. However, frequent acquisition slots increase the reset noise component and the dead time, since the detector is insensitive during the read out. When minimizing the dead time by increasing the read out speed, the read out noise increases, thus limiting the sensitivity of the system.

Integrating read out is largely used (e.g. image plates, CCDs, flat panels) since it does not impose strong requirements on the sensors and indirect detection techniques can also be applied.

On the other hand, photon counting devices reduce the read out noise and the dead time due to read out essentially to zero, but impose strict limits on the maximum input flux [10]. SPC (Single Photon Counting) sensors have to be chosen in order to provide the highest possible signal for each particle to be detected, and this is usually done by using semiconductor materials (e.g. Si, GaAs, CdZnTe) or gas avalanche detectors. The signal collected from the detector element is then compared with a threshold in order to discriminate it from the electronic noise and then counted. Several thresholds can be implemented in order to obtain energy resolution capability, allowing one to perform spectral analysis.
The main advantages of counting systems are:

- Contrast maximization, since low energy photons, which carry the contrast information about the detail, have the same weight as high energy ones, that in integrating devices degrade the image quality. An absorbed high energy photon deposits a relevant fraction of energy, and since there is small intensity variation of high energy photons intensity in proximity of the detail, in integrating systems they result as a constant component which is added to the signal due to the low energy photons. This constant component is present also in counting system, but its weight is lower since it is not proportional to energy;
- Signal-to-Noise ratio maximization, since the only source of fluctuation on the number of detected photons is given by the Poisson statistics;
- Perfectly linear behavior and virtually unlimited dynamic range, since the increment of the counters is linear and the dynamic range can be defined independently from the characteristics of the sensor (i.e. there is no saturation).

The noise of a correctly operated counting system is virtually zero. It depends only on the threshold level and will be described in detail in section 3.4, where the working principles of the read out electronic chain will be discussed.

The main limitation when using photon counting systems is given by their rate capability: if a second photon arrives during the time required to record the previous one, it might generate a loss of efficiency of the detection system [85, 86]. The phenomena that determine this effect will be described in section 3.4.

A loss of efficiency corresponds to a loss in the contrast resolution of the imaging system. If the detection system efficiency does not depend on the impinging X-ray intensity, the contrast of a detail is given by equation 1.3. Taking into account the efficiency loss of the electronics at high rates the measured contrast becomes [11]:

\[ C_m = \frac{\varepsilon(I_1) I_1 - \varepsilon(I_2) I_2}{\varepsilon(I_1) I_1} = C + \frac{\varepsilon'(I_1)}{\varepsilon(I_1)} I_1 C \]  

(2.12)

which is valid for low contrast details and is obtained by expanding in series the efficiency as a function of the detected intensity. \( C_m \) results lower than \( C \) since the derivative of the efficiency is negative and the contrast ranges between 0 and 1. The difference between the theoretical and the measured contrast is a function of the theoretical contrast itself. The loss in contrast is smaller for lower contrast details.

Because of these characteristics the choice of photon counting devices should be preferred to the integrating ones in particularly in presence of low intensities since a better image quality can be obtained with a smaller number of X-ray quanta, thus limiting the dose.

2.5 Existing Digital Mammography Detectors

In this section a brief overview of digital detectors used for clinical mammography will be presented.

i. Image plate

This kind of system is based on photostimulable phosphors and is probably the most widely used digital system for radiography since the beginning of the '80s [57].

The phosphor used is usually barium fluorohalide (BaFX:Eu, where X is a halogen, usually a combination of Br and I), which contains traps in the form of atomic energy levels of the Eu activator, where e-h pairs created by the X-rays are stored [87]. The system is contained in a cassette and after acquisition it is read out by a custom device: the storage phosphor is irradiated with red laser light and emits deexcitation blue light [29]. Erasure of the storage phosphor is
performed by intense illumination by visible light before it can be used again.

The pixel size of image plates is usually $100 \times 100 \, \mu m^2$ but $50 \times 50 \, \mu m^2$ can be achieved by using a higher sampling frequency. The phosphor is composed of fine grains in order to enhance the image sharpness by reducing the structured noise.

These systems can be designed with single or double sided reading [88]. In systems with double side reading the phosphor is deposited on a transparent support, thus the blue light emitted can be collected on both sides. The extra-light and increased thickness of the phosphor increase the efficiency and sensitivity of the system.

### ii. CCD

The use of CCD (Charged Coupled Device)s is well established in photographic imaging and is frequently used also in digital mammography, where the devices are coupled to a phosphor [29, 89, 90, 91].

Due to the technical problems and high costs in manufacturing large area devices, these detectors are often used for stereotactic imaging, where the field of view is only few cm, or tiled together in scanning systems, coupled to the phosphor via a demagnifying fiber optic taper [92, 93].

CCDs are characterized by a very small pixel size, that can be down to few microns, although the spatial resolution is often degraded by the light spread in the phosphor. Moreover these systems are affected by dark noise so that cooling is usually needed. However, the greatest disadvantages of this kind of system are the long read out time and the need of shielding the device from X-rays during the read out. The charge is in fact transfered from one pixel to its neighbor down to the read out line. This problems have been partially solved with the development of scanning system with TDI (Time Delay Integration) read out. TDI sensors have several parallely arranged photosensitive lines. The visual information is synchronously moved with the movement of the object to be scanned from one line to the following one. Beside a noise reduction, there is much higher sensitivity [94].

### iii. Amorphous silicon flat panel

aSi (Amorphous Silicon) flat panels are the state-of-the-art detectors for digital mammography [8, 29, 66, 95].

One advantage of these systems is that they can be made large enough for full field DM. The active matrix is a large area integrated circuit consisting of many TFT (Thin Film Transistor) [96]. The photons are converted inside a phosphor, which is generally evaporated directly on the sensor [97]. A photo-diode of amorphous hydrogenated silicon converts light to electric charge on the storage capacitance of each DEL. The TFT is connected to a data-line for read out and digitization. When the sensor is exposed, all the switches are in “off” state, while during the read out the switches are activated row by row and the charge is sent to the readout electronics where it is amplified and digitized. The detector is thus sensitive also during the read out phase. However, acquisition rates up to 30 frames/s can be achieved [98].

The TFT and other electronics occupy part of the pixel area, thus reducing the sensitive area of the detector. The ratio between the photodiode and the pixel size gives the fill factor (usually between 50 and 90%), which decreases when the pixel size is decreased. Standard pixel sizes for detectors based on such a technology are 100 $\mu m$ or 50 $\mu m$, but the resolution is affected by the use of scintillating phosphors.
iv. Amorphous selenium flat panel

Flat panels with aSe (Amorphous Selenium) as conversion element allow high efficiency direct conversion of X-rays [68, 69, 99]. When aSe is hit by X-rays, the e-h pairs created can be guided to the photo-conductor surface by the applied electric field. The charge is then collected by electrodes with an electronics similar to the one used in aSi flat panel.

Since the field lines can be bent, the charge is collected more efficiently and the fill factor can be kept close to 100%. The pixel size can thus be reduced without loss of geometrical efficiency [100]. Thanks to its high atomic number, the conversion efficiency in the mammographic energy range is high and this feature, together with the increased spatial resolution due to direct conversion, leads to a better image quality at parity of dose with respect to aSi flat panels. However, since the average charge created by a 17 keV X-ray is 500 e−, aSe is not feasible for photon counting.

The readout can also be implemented with CMOS (Complementary Metal-Oxide Semiconductor) sensor arrays [101] and selenium can be replaced with other photo-conductors such as PbI2 and HgI2 [102].

v. Silicon counter array

This kind of system will be reviewed in detail in chapter 3. The sensor consists in a silicon microstrip detector oriented with the strips parallel to the incoming radiation (edge on geometry), so that the absorbing length is given by the strip length, that can be up to several cm [6, 11, 103, 104, 105, 106]. The pixel size is determined by the strip pitch (down to 50 µm) times the detector thickness. Several detectors are tiled together in order to cover a larger area. A 20 keV photon creates in silicon about 5500 e-h pairs, which are then collected by the strips. The charge produced by photons is discriminated from the electronics noise in a counting modality. Thanks to the high absorption efficiency and the absence of anti-scattering grids, examinations can be performed with 1/5 of the dose with respect to traditional SF systems [107].

vi. Gas counter array

The use of gas detectors allows one to amplify the charge created by the X-rays through avalanche phenomena, allowing the use of counting techniques.

Parallel plate avalanche chambers with a segmented anode have been tested for X-ray imaging applications [108]. The chambers have a thin gap filled with krypton and a strong electric field induces the avalanche multiplication of the charge produced by the X-rays.

The problem of the low absorption efficiency of gases can also be solved by using long absorption length in an edge on geometry, where the gas chamber electrodes are oriented parallel to the impinging beam. This kind of detection system consists is 50 µm RPC (Resistive Plate Chamber) filled with gas at atmospheric pressure [79, 109, 110]. The X-rays convert in the RPC length with an efficiency of about 80% and the charge created undergoes a fast avalanche before being collected and discriminated by the counting read out electronics. The amplitude of the signal is independent from the photon energy and the requirements on the read out are less stringent than with semiconductor detectors, where the avalanche stage is not present. The detector can achieve a rate capability of 10^7 Hz/cm^2, about 1 kHz/pixel

Experimental studies on the performances of MICROMEGAS and multistage GEMs are being carried on [110]. Some interesting results are being obtained also with micro-channel plate detectors [80].
2.6 SUMMARY

So far the introduction of digital X-ray mammography has been very slow compared to most other X-ray examinations due to high costs and technical challenges to meet the high demands on image quality and dose in mammography as well as the demands on specialized workflow support for screening mammography [57].

Digital mammography systems are currently commercially available, both with a small area and with full field technique. The development of full field digital systems is now intense, as well as the development of dedicated workstations, computer aided diagnosis and other special techniques. Hard copy reading of digital mammograms has been the most common display mode so far, but to take full advantage of the digital concept, diagnostic as well as logistic, soft copy reading must be applied.

Full field DM is equivalent or better than SF mammography in the detection of calcifications and low-contrast objects in mammograms at about the same dose. Due to the higher DQE, there is a potential of DM systems for significantly higher image quality or significantly lower dose than conventional ones [8].

A lot of R&D work is being carried on the development of innovative systems that exploiting their direct conversion capability or a photon counting technique could still improve the image quality to dose relationship with respect to commercially available digital systems [14, 68, 79, 107].

The investment costs are much higher for digital than screen-film mammography today. Nevertheless digital mammography will most likely replace screen-film mammography to a large extent, especially in large-scale operations.
3. EDGE ON SILICON SENSORS WITH SINGLE PHOTON COUNTING READ OUT

The detectors developed during this work are based on side illuminated silicon sensors with single photon counting read out.

In this chapter, after highlighting the main properties of silicon and the features of microstrip sensors, the edge on configuration for efficiency enhancement will be described. The main requirements for microstrip detectors read out will be shown and the electronics used for photon counting, with the advantages already highlighted in section 2.4, will be discussed, with some examples of existing detection systems.

3.1 SILICON MICROSTRIP DETECTORS

Silicon microstrip detectors are largely used in many fields of physical research [111]. The search for a new semiconductor material to replace silicon has not been successful yet because of the wide diffusion of the techniques for the fabrication of silicon sensors and electronics devices [112].

In this section the properties of silicon as a detecting material will be discussed. The working principles of microstrip detectors will be described and the main issues of sensor design will be pointed out.

i. Basic properties of silicon

Semiconductors are crystalline materials whose outer shell atomic levels exhibit an energy band structure with a small forbidden gap. An exhaustive description of their properties can be found in [25, 113].

Charge transport in a semiconductor is due to both electrons and vacancies (holes). The number of intrinsic charge carriers depends on the temperature and on the energy gap between valence and conduction band in the material. In silicon the energy gap is 1.1 eV and the intrinsic carriers concentration at room temperature results \(1.5 \cdot 10^{15} \text{ cm}^{-3}\) [114].

In pure semiconductor crystals the number of electrons is equal to the number of holes in the conduction band. This balance can be changed by introducing a small amount of impurity atoms having one more (donors) or less (acceptors) electron in their outer atomic shell. The dopants integrate themselves into the lattice and introduce an additional energy level in the forbidden energy gap between the valence and conduction band. The presence of a level inside the forbidden gap shifts the Fermi level of the semiconductor.

In the case of donors the level is close to the conduction band, thus creating an excess of conduction electrons, while the acceptor level is close to the valence band and causes an excess of holes as charge carriers. A semiconductor doped with donors (n-type semiconductor) has electrons as majority carriers, while when the dopant is an acceptor (p-type semiconductor) the majority of charge carriers are holes.
**ii. The p-n junction**

All semiconductor detectors are based on the formation of a junction, usually obtained from the juxtaposition of an n-type with a p-type semiconductor (figure 3.1.(a)) [111, 115, 116]. Because of the difference of the Fermi level in the two materials, electrons drift to the p side, while holes drift to the n side. The result is a charged region depleted from charge carriers near the junction, as shown in figure 3.1.(b),(c). This region is known as depletion region, or space charge region. The charge distribution generates a built-in electric field and thus a potential difference $V_0$, known as contact potential, generally of the order of 1 V.

Charges created or entering the depletion region will be swept out of it by the electric field.

The electric field and potential as a function of the depth inside the junction are shown in figure 3.1.(d),(e).

The depletion depth can be tuned by applying an external potential to the sides of the junction. When a positive voltage is applied to the p-type and a negative one to the n-type side (direct-bias) the depletion region size will decrease until the semiconductor starts behaving like a conductor. At the opposite, when a reverse bias is applied (negative to the p-side and positive to the n-side) the depletion zone will be enlarged. The potential difference $V$ will be given by $V_0 + V_B$ where $V_B$ is the external reverse bias voltage applied. It can be shown that the depletion region is proportional to $\sqrt{V}$.

The depletion layer has also a certain capacitance, that can be easily calculated as the capacitance of a plane plates capacitor with distance equal to the depletion depth $d$ and is inversely proportional to $\sqrt{V}$, reaching a constant value when the detector is fully depleted.

**iii. Silicon detectors**

The primary advantage of semiconductors over other detectors is the very small average energy needed in order to produce an electron-hole pair. The required energy is about 3.6 eV for silicon, about one order of magnitude less than in gases and two orders of magnitude less than in scintillators [117].

When a charged particle crosses a p-n junction (or a photon is absorbed in it) the deposited energy creates e-h pairs, that start drifting to the electrodes under the influence of the applied electric field.

The bias is usually chosen so that the depletion region extends throughout the silicon bulk in order to maximize the size of the region sensitive to radiation and to reduce the noise.

The junction can be segmented as in microstrip detectors, in order to obtain position resolution and decrease the sensor capacitance. The charge cloud drifts to the closest strip (figure 3.2) and all the strips behave as independent junctions. Common strip pitches are as low as 50 $\mu$m and the resolution is almost independent from the strip width.

Common microstrip detectors consist in highly doped p strips (p$^+$ doping) on the surface of n doped bulk. The fabrication techniques of silicon detectors are described in detail in [111].

The strip capacitance is given by the sum of the junction capacitance and the inter-strip capacitance. The first one depends on the strip width, while the second one depends on the inter-strip distance (i.e. difference between strip pitch and strip width). The inter-strip capacitance is usually at least one order of magnitude higher than the junction capacitance.

Electrodes are deposited on the strips. Sometimes the strips can be AC (Alternate Coupling) coupled to the read out electronics by interposing an oxide layer between the strips and the metal. The coupling capacitance is much higher than that of the strip and can be neglected in the total calculation since the two are connected in series.

The strips can be biased through resistors connected to a common bias line. The polysilicon resistors value needs to be high (in general >20 M$\Omega$) and uniform enough in order to obtain good noise performances and avoid cross talk between the strips.
Fig. 3-1: (a) Sketch of a p-n junction and plots of (b) charge carriers concentration and (c) charge density distribution, (d) electric field and (e) electric potential as a function of the distance from the junction.
Another biasing technique is the so called FOXFET biasing, which exploits the punch-trough effect of a completely separate biasing structure [118, 119].

A $n^+$ doped layer is needed on the backplane of the detector in order to apply the positive bias voltage

\[ iv \quad \text{Noise of microstrip detectors} \]

The noise of a microstrip detector is mainly due to three terms [120]:

- Shot noise created by the leakage current of the detector, mainly due to the intrinsic leakage current $I_{dark}$ flowing through the junction. $I_{dark}$ is given by the sum of three terms: (i) Surface current due to the charges moving on the crystal surface: it is mainly determined by the detector fabrication technology and can be limited by the use of guard structures; (ii) Diffusion current due to the carriers diffusion from the undepleted regions of the semiconductor: it depends on temperature and on the depletion depth and it is usually negligible at room temperature and full depletion of the detector; (iii) Bulk current due to the charges thermally generated in the depletion region under the effect of the electric field: it strongly depends on the temperature and on the applied bias voltage and it is proportional to the detector volume.
- Thermal noise from the detector biasing resistors. The spectral current density is proportional to the inverse of the resistance value and is negligible when the potential drop across the bias resistor due to the leakage current is of the order of 50 mV [117].
- Series resistance noise due to the metal strip resistance. The spectral power density is proportional to the strip resistance.

The leakage current and biasing resistors component introduce parallel noise, while the strip resistance introduces thermal serial noise.

All the three sources of noise are white i.e. do not depend on frequency.
3.2 Edge on silicon sensors

The main problem related to the use of silicon strip detectors for medical X-ray imaging is that the absorption length of silicon in the energy range 10-100 keV is of the order of (or larger than) one mm so that only a small fraction of the X-rays are converted in the commonly used 300 \( \mu m \) thick detectors when the radiation impinges on the surface of the detector (face on configuration). This low absorption efficiency means that the undetected radiation increases the dose to the patient without contributing to the image formation.

Moreover, when using double sided detectors with crossed strip to acquire a two dimensional image, the read out needs to be faster than state of the art electronics in order to avoid ambiguities for multi-hit events [121, 122, 123, 124]. These problems can be solved by orienting the detectors with the strips parallel to the incoming X-ray beam [9].

i. The edge on configuration

The edge on geometric configuration was first proposed by the SYRMEP collaboration [125, 126] and is sketched in figure 3-3a.

The pixel size is given by the strip pitch \( p \) times the detector thickness \( t \). The absorbing thickness is therefore given by the full strip length \( l \), that can be of several cm. The main limitation on the efficiency of the detector is given by the size of the undepleted region which is present in the entrance window of the detector between the end of the strip implants and the edge of the detector. The thickness of this region is mainly defined by the distance \( d \) between the end of the strips and the scribe-line. This cutting distance is usually about 1.5 times the wafer thickness in order to limit the leakage current due to the cut, but can be reduced by using innovative fabrication methods [127, 128, 129]. The size of the undepleted region is usually smaller than \( d \) and can be tuned by changing the bias voltage of the detector [130]. Figure 3-3b shows the efficiency of a 1 cm strip long detector with standard cutting distance of 450 \( \mu m \).

The efficiency of the detector in edge on orientation is much higher than in face on configuration and generally higher than the one of conventional screen-film systems, resulting in a significant reduction of the patient dose.
The X-rays are converted into electric signal without the intermediate step of conversion into visible light with the advantages already highlighted in section 2.2. The edge on configuration determines an essentially 1D detector and scanning is required with the consequences pointed out in section 2.3.

ii. Overview of existing edge on detectors

In this section a brief overview of some projects using edge on detectors will be presented. The experiments described are active in the field of spinal radiography and mammography. Some detectors are used in a slit-scan geometry in conjunction with an X-ray tube as shown in figure 2-3. Since the divergence of the beam is not negligible, the detectors are designed with a slight strip fan out in order to avoid any parallax problem. The SYRMEP detector, optimized for SR mammography will be described in detail. The differences on the detector design resulting from the different requirements of the examination will be discussed.

a. Spinal radiography

Spinal cord X-ray imaging is commonly used for the diagnosis of vertebral lesions. This type of examination is usually performed with the patient standing. The area to be imaged is about 50×120 cm² wide. A resolution higher than 1 mm is required and the optimum X-ray energy for the examination is about 50 keV.

A “quantum X-ray radiology apparatus” based on a silicon microstrip detector in edge on configuration was optimized for spinal radiography by B. Hilt et al. [131, 132]. Both the thickness of the silicon sensor and the strip pitch are 500 µm. The strip length is 5 cm, corresponding to a stopping power of more than 90% for 50 keV photons. Signal processing is performed by an analog ASIC followed by a digital one [133].

Eight detectors are arranged in a linear array covering a length of about 50 cm with a dead zone of only three strips between the modules. Dose measurements show that with this detection system it is possible to reduce the dose given to the patient by at least a factor of ten. A second version of the apparatus with an optimized geometry, improved spatial resolution and spectroscopic capabilities is under development.

b. Digital mammography

The requirements of a mammographic detection system have been described in detail in chapter 2. A mammographic examination is usually performed in the 15-20 keV energy range so the absorption due to the undepleted region can be very strong.

Several experiments of reducing the cutting distance have been performed at the Jožef Stefan Institute in Ljubljana (Slovenia) [134, 135]. The prototype detectors used have a strip length of 4 mm, a thickness of 220 µm and a strip pitch of 100 µm. The detectors were tested on wafer and with cutting distances between 400 µm and 136 µm [104]. An increase of leakage current of one order of magnitude at full depletion voltage has been observed only for the detector cut at 136 µm. However, all detectors were operated without any observable increase of noise when connected to SPC read out electronics [136]. The resulting efficiency of the detector is of about 90% for 22 keV X-rays.

Instead of reducing the cutting distance, researchers of the Royal Institute of Technology in Stockholm (Sweden) have proposed to tilt the detector in front of the beam in such a way that the device is irradiated beside the undepleted region, as shown in figure 3-4 [105, 137, 138]. The resulting effective dead layer ranges between 20 and 50 µm. Some of the higher energy photons escape from the backplane of the detector but lower energy ones are totally absorbed.
This approach is particularly effective when a polychromatic beam from an X-ray tube is used and the low energy component is considerable.

The strip length of the detectors is 1 cm and, after the optimization of the tilt angle (about 4.5°), the detection efficiency is of about 95% [105, 106]. The dose can be reduced down to 1/5 than in a conventional mammographic examination [107].

The strip pitch of the detectors is 50 μm, and the vertical pixel size is reduced to 50 μm by means of a slit placed in front of the detector. Several detectors are arranged in a grid in order to reduce the scanning time.

The X-ray beam is focused on the detector by means of X-ray lenses in order to reduce the scanning time and the heating of the X-ray tube [81, 82].

This detector is now produced by Mamea Imaging AB [139] and commercialized by Sectra AB [107].

c. The SYRMEP detector

The research and development studies on edge on detectors with SPC read out started at the beginning of the '90s [125]. The detector is optimized for synchrotron radiation applications. Scanning is not a disadvantage in this case, because the sample movement is intrinsic in the SR setup. In order to exploit the maximum beam dimension it is necessary to stack several detectors together. Tilting the multi-layer detector would not be an effective way of increasing its efficiency since the upper layers would shield the lower ones and the spatial resolution of the detector would be degraded. Since the beam divergence is negligible, the strips of the detector are parallel.

The first detector prototype had 500 × 500 μm² pixel and only 15 channels were equipped with discrete read out electronics [126]. The detector has evolved in order to prove the feasibility of clinical examination with SPC edge on detectors.

An AC coupled FOXFET biased detector has been developed [6]. The strip length is 1 cm, while, on the basis of simulations and measurements on design structures, the cutting distance has been fixed to 250 μm [130]. The average undepleted thickness has been evaluated from efficiency measurements to be less than 150 μm. The overall efficiency is about 80% at 20 keV. The pixel size is 200 μm in the horizontal direction and 300 μm in the vertical one, but the vertical resolution can be improved by scanning the sample in front of the beam with a step smaller than the wafer thickness [140]. A filtered deconvolution algorithm is then applied to the acquired data. In this way, the spatial resolution obtained is determined by the scanning step rather than by the pixel size.

Figure 3-5 shows how the sensors are assembled in order to obtain a multi-layer module [141, 142]. The detectors were designed with an innovative trapezoidal geometry. “Full” structures are alternated to layers of “half” structures in order to allow enough space for the wire bonding to the read out electronics and power supply [130]. A three layer prototype has been assembled and tested [45]. The overall statistics of the image is obtained by summing up the information of corresponding pixels belonging to different layers, thereby reducing the acquisition time and the negative effects due to noisy or dead pixels [143]. The pixels in superimposed layers are aligned with a precision of about 10%, and the space between the two half modules is of only two strips [45]. A distance of 50 μm was kept between the layers by using kapton foils of the same thickness with holes for
glue dripping as spacers, avoiding cross-talk effects. The width of the prototype is about 5 cm, but it would be possible to place several modules tiled in order to cover a wider area.

Further improvements of the sensors will be described in section 4.1.

The high efficiency of the SYRMEP edge on detector allows the acquisition of medical images using phase techniques still delivering a low dose to the sample [44]. The pixel size has been reduced to 100 µm by means of a slit in order to detect the narrow interference peaks. Moreover, the use of a three layers detector makes it possible to simultaneously acquire images based on different techniques (e.g. absorption, diffraction enhanced, small angle scattering) on different detector layers by means of a specific setup [45]. This technique results in an increase of the information extracted from the sample without increasing the dose delivered.

A feasibility study of breast computed tomography on in vitro tissues has been carried out with promising results and will be reviewed in detail in section 5.1 [65].

3.3 FRONTEND ELECTRONICS FOR X-RAY DETECTION

X-rays absorbed in a silicon detector usually interact by photoelectric effect [27]. The charge created is of only a few thousand e-h (about 5500 e-h for a 20 keV photon) and must be collected by the read out electronics.

It is then important that the charge collection efficiency is good and the read out electronics does not add noise to the signal at the amplification and shaping stages.

The signal processing is usually performed by integrated circuits [144].

i. Charge preamplifier

The first operation performed by the electronic chain is to amplify the charge collected from the detector [145]. A charge sensitive preamplifier is commonly used. It usually consists in an OP-AMP (Operational Amplifier) with capacitive feedback, as shown in figure 3-6a.

We can consider that the charge \( Q \) is stored on the feedback capacitor \( C_F \) and thus the output voltage \( V_{out} \) results:

\[
V_{out} = -\frac{Q}{C_F} \quad (3:1)
\]

A large value resistor \( R_F \) is inserted in parallel with \( C_F \) in order to discharge the capacitor. The falling edge of the signal will behave like a negative exponential with time constant \( \tau = R_F \cdot C_F \).

Since the feedback capacitance is usually about 1 pF and the resistor is of the order of some MΩ, the discharge time constant results of the order of some microseconds and the signal needs a reshaping in order to support high rates.

It is important to notice that trying to change the \( R_F \) and \( C_F \) values to improve the rate response results in higher noise when decreasing the resistance and lower gain when decreasing...
The capacitor value.

**ii. Signal Shaping**

Shaping is usually obtained by means of simple resistive and capacitive nets behaving as a band-pass filter [145]. Figure 3-6b shows a simple CR-RC filter with pole zero cancellation.

The CR filter at the beginning of the chain \((C_1, R_1)\) basically derives the input signal and the response to the signal coming from the discriminator results in a falling exponential curve with a time constant that can be arbitrarily decreased. However the tail of the signal results in an undershoot, so a pole zero resistor \((R_{PZ})\) is needed in parallel to the capacitor in order to avoid the baseline shift. The signal decay constant can be chosen short enough in order to improve the rate capability of the detector. However if the signal decay is too fast, it is difficult to detect the peak of the signal. An RC filter \((R_2, C_2)\) behaving like an integrator usually follows so that the signal decay at the shaper output results slower. Often several orders of CR-RC filters are used in order to improve the shaping of the signal.

The peaking time of the signal can then be a good estimate of the rate capability of the system, but often a compromise has to be found in order not to decrease the signal height.

The time decay characteristic of the signal is called shaping time and plays an important role in order to evaluate the speed and noise performances of the system.

**iii. Noise**

Solid state detectors readout implies the measurement of charge delivered by a capacitive source \(C_D\) that corresponds to the detector capacitance, as shown in figure 3-6a [145]. An infinitely narrow distributed charge \(Q\) from the detector would appear at the amplifier output as a gaussian distribution of standard deviation \(ENC\) (Equivalent Noise Charge). The \(ENC\) gives an estimate of the noise of the detection system and is usually expressed in units of \(RMS\) (Root Mean Squared) electrons.

The noise of the readout electronics is mainly due to three terms dependent on the input transistor fabrication [111]:

- Flicker noise,
- Channel thermal noise,
- Bulk series resistance noise.

All the terms are considered to be in series with the input transistor and the first has a \(1/f\) dependence while the others exhibit a “white” behavior.

The overall noise of the detection system will be given by [120]:

\[
ENC^2 = ENC_{detector}^2 + ENC_{readout}^2
\]  

(3.2)
Fig. 3-7: Simulation of the signal formation inside a counting system: first the photon distribution is created, the noise is added and then the signal is propagated with a doubly triangular shape.

\[ ENC = (ENC_{\text{leakage}}^2 + ENC_{\text{polarization}}^2 + ENC_{\text{metal}}^2) + (ENC_{\text{flicker}}^2 + ENC_{\text{channel}}^2 + ENC_{\text{bulk}}^2) \]

All noise terms in series (i.e. detector metal strip resistance, transistor flicker, channel and bulk resistance noise) are proportional to the detector capacitance. The noise of the detection system is then proportional to the detector capacitance and can be expressed as:

\[ ENC = A + B \cdot C_D \]  

(3:3)

\( A, B \) depend both on the shaper settings, as all the noise sources do.

3.4 SINGLE PHOTON COUNTING

The main advantages of the use of a counting system with respect to an integrating one have already been pointed out in 2.4.

In this section the behavior of the comparator, that digitizes the signal, will be described and the major issues in the operation of counting read out electronics will be highlighted.

A simple simulation of the behavior of a counting system has been performed. Noise and signal events have been generated with a random number generator. The shaping is simulated by convolving the input signal with a shaping function, as shown in figure 3-7. The signal with a positive triangle and the undershoot with a negative one. The approximation is certainly poor but it allows to extract some interesting data about the behavior of the counting system.

The main parameters for signal generation (e. g. rate, amplitude) and shaping (e.g. rising and falling time, undershoot amplitude and duration) can be selected through a Graphical User Interface (GUI). The simulation program is written in C [146, 147].
i. Comparator

A comparator is basically given by an open-loop OP-AMP (i.e. without feedback) [148]. If the signal $V$ is higher than the threshold level $V_{\text{thres}}$, the output is driven to the positive supply voltage, while it is driven to the negative supply voltage if $V < V_{\text{thres}}$. The switching time is limited by the slew rate of the OP-AMP.

In order to stabilize the switching against rapid triggering by noise as the signal fluctuates around the threshold level, a Schmitt trigger is often implemented [149]: negative feedback is used to prevent switching back to the other state until the input passes through a lower threshold voltage.

A flash ADC (Analog to Digital Converter) can be designed as a net of resistors and comparators with encoding logic [150], thus the circuit design rules used for analog to digital conversions should be applied also to counting systems.

ii. Noise in single photon counting systems

A well operated photon counting system is virtually noise-less.

However, since the electronics noise events have a gaussian distribution with a standard deviation $\text{ENC}$, the probability that an event is higher than the threshold is finite and will be given by [151]:

$$P = \int_{Q_{\text{th}}/\text{ENC}}^{+\infty} e^{-\frac{x^2}{2\text{ENC}^2}} \, dx = \frac{1 - \text{erf}(Q_{\text{th}}/\text{ENC})}{2} \quad (3:4)$$

Where $Q_{\text{th}}$ is the threshold value expressed in signal charge.

If one considers white noise, its average frequency will be defined by the shaper settings and we can approximate it with half the inverse of the shaping time $T_s$.

The number of noise counts $N_{\text{noise}}$ in a time interval $\Delta t$ will then be:

$$N_{\text{noise}} \sim \frac{\Delta t}{2T_s} \frac{1}{2} \frac{1 - \text{erf}(Q_{\text{th}}/\text{ENC})}{2} \quad (3:5)$$

An increase of the rate capability of the system by decreasing the shaping time of the signal worsens the noise characteristics of a counting system because the noise detection rate is increased.

The presence of noise, however affects also the detection capability of photons, since their signal also have height fluctuations with standard deviation given by the ENC, so that some photons will be lost. The threshold value will then have to be placed at a level considerably higher than the ENC, but still lower than the signal height.

The behavior of the counting system for different ENC values has been simulated. Figure 3-8 shows threshold scans simulated for various ENC values, a shaping time of 250 ns and 100 kHz photons with Poisson-like distribution. It is clear that the $\text{SNR}_{\text{signal}}$ must be greater than 4 in order to correctly operate the counting system.

iii. Flat field correction

A detector usually present disuniformities which are caused by sensitivity fluctuations of the electronics or of the sensor over the active area [10].

The correction of pixel-to-pixel variations is important in order to increase the visibility of the details in the image as discussed in section 2.1.

One of the reasons for a non-uniform threshold distribution is the area-dependent mismatch between transistors, which affects both gain and ENC of the channel. This does not seem to play a major role for a counting system if the threshold is set comfortably above noise and below the beam energy, while threshold adjustment is essential for applications with threshold settings close
Disuniformities of the electronics can be corrected by calibrating each pixel individually. This can be obtained by using a threshold tuning circuitry in order to adjust the threshold on a channel by channel basis narrowing the distribution on the whole detector.

The sensor can contribute to the non-uniformities because of local fluctuations in material resistivity, doping, impurity and defect level distribution [152]. These characteristics can affect the radiation absorption, charge creation and collection in the sensor.

These differences are usually corrected by means of a flat field correction as described in section 2.1. This method is effective in most cases though it shows some limitations in case the beam is polychromatic, due to the beam hardening after the sample [153].

If the detector response depends on the signal rate, flat fields must be acquired over a range of intensities.

**iv. Charge sharing**

Some problems can occur when the charge cloud generated by a single photon is spread over several pixels [105]. In this case the behavior of the device depends on the threshold settings: if the threshold value is high, the photon will not be counted in any of the pixels, while if it is low the signal could be higher than the threshold in several pixels and then counted by many of them.

In order to overcome the problem, the ideal threshold value should be exactly half of the pulse height, so that the signal would be assigned to only one pixel. This is not possible when using polychromatic beams because different energies correspond to different signal heights, but it is very difficult even with monochromatic radiation because of noise and disuniformities between channels.

The charge sharing imposes limits on the size of the pixels that should not be smaller than 50 µm.

The only way of fully overcome this problem is to keep a low threshold and analyze the presence of coincidences between neighboring channels. An improvement of the spatial resolution of the detector could come from the search of the center of mass of the signal, that can be obtained with a amplitude resolution for signals in coincidence over neighboring channels. However this
improvement of the detection system would also require an enhancement of the rate response and a reduction of noise.

v. Rate capability

The dependence of a counting system performances from its rate response have been described in section 2.4.

In counting systems, the loss of efficiency at high rates is mainly determined by signal pile-up and baseline shift, as shown in figure 3-9. When the signals pile up in the region around the peak of the signal, a loss of efficiency can be observed at low threshold value, while in the second case, where the latter signal rises upon the undershoot of the first, the efficiency loss can be measured at high threshold value. An optimization of the threshold level is then important in order to improve the behavior of the system and has to be made as a function of rate and pulse height. The pile up determines a paralizable behavior of the detector, with a dead time of the order of the shaping time, while the baseline shift effect has a mixed behavior since its dead time is delayed from the event [115, 116].

The response of a counting system to various photon rates has been simulated. Figure 3-10a shows the signal waveform at different rates, as obtained from the simulation for a peaking time

![Waveform](image1)

![Threshold scan](image2)

Fig. 3-10: a) Simulation of the signal at the entrance of the comparator at different rates and b) Threshold scans of a counting system with various photons rates. The peaking time has been set to 250 ns, the shaping time to 1 μs and the undershoot to 10 % of the signal amplitude for 500 ns.
Fig. 3-11: Simulated efficiency of a counting system a) with different shaping settings ($T_p=100$ ns, $T_s=500$ ns, $T_u=250$ ns, $U=10\%$; $T_p=250$ ns, $T_s=1$ µs, $T_u=500$ ns, $U=10\%$; $T_{peak}=500$ ns, $T_s=2$ µs, $T_u=1$ µs, $U=10\%$) and threshold set at half of the signal amplitude; b) different threshold settings (half, equal to and 1.5 times the signal amplitude) with shaping settings as in figure 3-10.

$T_p=250$ ns, a shaping time $T_s=1$ µs and an undershoot amplitude $U=10\%$ of the PH (Pulse Height) and duration $T_u=500$ ns. Figure 3-10b shows the simulated threshold scans of the same counting system as a function of the impinging Poisson-like rate. With these settings the signal pile-up is the most important effect, resulting in a loss of counts at low threshold values. However, the pile-up determines an increase of counts at high rates for thresholds higher than the signal amplitude.

Figure 3-11a shows the efficiency of the counting system for three different shaping settings ($T_p=100$ ns, $T_s=500$ ns, $T_u=250$ ns, $U=10\%$; $T_p=250$ ns, $T_s=1$ µs, $T_u=500$ ns, $U=10\%$; $T_{peak}=500$ ns, $T_s=2$ µs, $T_u=1$ µs, $U=10\%$) and threshold set at half of the PH.

The data have been fitted with the efficiency function of a paralizable detector and the resulting dead time are 350 ns for the fast settings, 800 ns for the intermediate ones and 1.5 µs for the slow settings. The results are compatible with the signal triangular shape and, with these settings, the predominant effect is the signal pile up.

Since the rate response of the detection system is very sensitive to the threshold settings, the efficiency of a counting device with different threshold levels has been simulated, as shown in figure 3-11b.

When the threshold is set at exactly PH, the efficiency is about 50 %, but the dead time results smaller than when the threshold is 0.5-PH since the time that the signal is over the threshold is shorter.

By setting the threshold higher than the signal amplitude, the simulated efficiency results very small at low rates, but increases with the photon intensity.

It is also interesting to point out that at high rates, the variance on the number of counts becomes lower than the mean [86]. Figure 3-12a shows that this effect is present for all threshold values. The variance and mean of the counts are calculated on 500 pixels.

Since the fluctuations on the number of counts become smaller with rate, the DQE (defined in equation 2:3) will increase at high rates. Figure 3-12b shows the DQE for threshold set at half of the signal amplitude, at exactly PH and at 1.5-PH.

Figure 3-13a shows the simulated measured contrast as a function of the counting rate for a
Fig. 3-12: a) Variance to mean ratio and b) DQE simulated for threshold set at half of the signal amplitude, at exactly the pulse height and at 1.5 times PH. The legend refers to the threshold settings, while the shaper settings are the same as in figure 3-10.

detail of theoretical contrast 10%. For threshold set at half of the signal amplitude or equal to PH the contrast gets lower with rate, as expected from equation 2:12. Since the efficiency for threshold set at PH is more constant with rate, also the contrast is less influenced by the photon flux. For threshold higher than the signal amplitude, the contrast results much higher than the theoretical one. This could also be expected from equation 2:12 since in this case the derivative of the efficiency as a function of rate is positive.

Figure 3-13b shows the FOM (defined in equation 1:5) calculated for a detail of 500 pixels and 10% contrast. It is expressed in arbitrary units since it is simply obtained by dividing the SNR\text{detail} for the square root of the number of photons generated by the simulation program. It is interesting to point out that at high rates the FOM is higher for higher thresholds.

Though with these settings the FOM never reaches the one obtained at low thresholds and low rates, it is possible to severely reduce the acquisition time. However the SNR\text{detail} can be increased by increasing the statistics using a slightly longer acquisition time. This is certainly a bad solution in medical imaging applications, where the dose given to the patient should be limited, but could help to reduce the acquisition time and increase the visibility of low contrast details for example in industrial imaging.

Moreover, an increase of the threshold could further enhance the SNR\text{detail} in noisy systems, where the presence of noise counts at low thresholds can determine a loss of visibility of the details.

The counted intensity cannot be directly used for evaluating the absorption coefficient of the sample (as needed e.g. in tomography) but has to be converted back to the real number of impinging photons. This operation is possible thanks to the high SNR\text{detail}, knowing the efficiency of the system as a function of rate.

Moreover the use of a threshold higher than the pulse height improves the contrast only in a well defined range of intensities and could not be used for applications where a very high dynamic range is required (e.g. diffraction experiments).

However, the implementation of a double threshold would allow a strong improvement of the rate capability of the system. Figure 3-14 shows the efficiency of the detection system obtained by summing up the counts collected with a threshold set at half of the signal amplitude, with those
Fig. 3-13: a) Ratio between measured $C_m$ and theoretical $C_t$ contrast and b) FOM simulated for a 10% contrast detail with threshold set at half of the signal amplitude, at exactly the pulse height and at 1.5 times PH. The legend refers to the threshold settings, while the shaper settings are the same as in figure 3-10.

The efficiency with such setup decreases at half the speed of the case with threshold set at half the pulse height. The loss of efficiency is due to the triple pile-up phenomena that arises at very high rates. Multiple thresholds can further enhance the rate capability. This implementation is relatively simple with monochromatic radiation. However, methods for increasing the electronics speed have been implemented also for the detection of polychromatic radiation [154].

Fig. 3-14: Efficiency of a counting system with threshold set at half and 1.5 times the signal amplitude and obtained by summing up the counts obtained at both thresholds. The shaper settings are the same as in figure 3-10.
vi. **Overview of photon counting ASICs**

In this paragraph a few existing SPC ASICs will be described in order to evaluate the state-of-the-art and compare their performances with the read out electronics used for this work. This review does not mean to be exhaustive and only few ASICs used for the read out of silicon strip detectors will be described. The attention will be focused on their limitations in order to highlight the R&D work that is still needed for the optimization of an ideal photon counting detector. The new ASIC FROST (Frontrad Read Out sySTem) developed for improving the SYRMEP detector performances will be presented in detail in the next chapter.

### a. CASTOR

CASTOR has been designed at LEPSI (France) in order to operate the SYRMEP microstrip detector [136].

The ASIC fabricated in 1.2 µm CMOS technology and is made of 32 channels each consisting of a charge preamplifier, a CR-RC shaper, a comparator and a 16-bit counter with serial readout.

The gain is 190 mV/fC while the ENC is 95 e− for a detector capacitance of 2 pF and the noise slope is 17 e−/fC [155]. The simulated peaking time is 850 ns, but the measured shaping resulted of several µs and the undershoot duration is of the order of 10 µs [143]. A loss of efficiency can already be observed with a rate of 10 kHz.

The ASIC has been largely used for the development of the SYRMEP detector, assembling a three-layer detector of 256 channels per layer, as described in section 3.2 [142].

### b. RX64

The RX64 ASIC has been designed for dual energy imaging in mammographic and angiographic examinations [156]. It is derived from the previous RX32 and COUNT32 ASIC [157].

The ASIC is formed by 64 channels, each consisting in a charge preamplifier, a shaper and a comparator. The signals are counted by 20-bit asynchronous counters. I/O (Input/Output) handling and acquisition controls are integrated on the ASIC.

The gain is in the range 370-650 mV/fC, while the ENC is 170 e− for a detector capacitance of 2.5 pF with 700 ns peaking time. The peaking time can range between 500 ns and 1 µs [158, 159, 160].

Prototypes of 128 and 384 channels have been assembled and tested. A new version of the ASIC with a double threshold is now under design.

### c. DIFFEX

DIFFEX is a module designed at CCLRC Rutherford Appleton Laboratories (UK) for the measurements of 5-20 keV X-rays in diffraction experiments at SR facilities [161].

The ASIC is formed by 64 channels, each featuring a low noise charge preamplifier, a CR-RC shaper, a discriminator, a 4-bit ADC and eighteen 15-bit counters for storage. The ASIC can work in photon counting mode. A high counting rate modality can be selected in order to enable a special dead time circuit to improve the counting rate capability. However it can also be operated as a 16 channels multichannel analyzer, with 15-bit capacity for each bin. A charge sharing check between neighboring pixels can be enabled and shared events are stored in separate counters. The energy spectrum is thus cleaned up by low amplitude events due to charge sharing and the spatial resolution is enhanced.

The readout can be carried on while acquiring new data for dead time free operation.

The ENC is 140 e− for a 2 pF detector capacitance and the noise slope is 40 e−/pF with 100 ns peaking time. The peaking time can be selected down to 50 ns. In this case the ASIC can operate
at rates higher than 1 MHz without energy resolution.

The detector module is obtained by assembling 16 ASICs, direct bonded to 1024 100 µm pitch microstrips [162], however there are no data about an installed DIFFEX system.

d. MYTHEN

MYTHEN is a module designed at the Swiss Light Source for diffraction experiments. Each ASIC consists of 128 channels each made of a charge sensitive preamplifier, two shapers, a single level comparator and a 18-bit pseudo-random counter. Each channel has a 4-bit DAC for the fine tuning of the comparator threshold [163].

The input pad pitch is 50 µm in order to allow direct bonding to the detector. The ASICs are designed in order to be daisy-chained. The ENC of the system is 240 e⁻ and the peaking time is of about 250 ns, allowing a maximum counting rate of 1.4 MHz.

A 15000 channels system is operating at the Swiss Light Source.

The ASIC was designed in DMILL (Durci Mixte Isolant Logico Lineaire) technology, but a new improved 0.25 µm CMOS version is now under test [164].

3.5 DISCUSSION

Edge on silicon microstrip detectors have been largely used for X-ray imaging applications due to their high efficiency in the energy range 10-100 keV. Interesting results regarding further efficiency enhancements can arise from novel manufacturing techniques [127, 128, 129]. The “active edge” fabrication technique has proved cutting distances as small as 15 µm, thus leading to almost 100% efficiency.

In this geometrical setup it is necessary to rely on scanning techniques. Due to these requirements, the main limitation connected with the use of edge on detectors in clinical examinations is the long duration of the acquisition. This problem has been overcome by assembling arrays of detectors covering large areas [45, 142] and by developing fast low noise read-out electronics, reducing therefore the time of each acquisition step [11, 143]. In this way the time of image acquisition is compatible with the constraints of a clinical examination.

The search for a new material to replace silicon in electronics has been active for years but has not been yet successful. On the sensor side, a lot of efforts have been spent on the development of GaAs pixel detectors [71, 72, 73, 165], but the only material different from silicon that is currently used in medical imaging is selenium [68, 69]. However, the low sensitivity of the photoconductor does not allow to perform photon counting read out.

Counting detectors allow the maximization of the visibility of the details in the image. The main issues in frontend electronics design are:

- the noise, in order to detect low energy photons;
- the speed, in order to exploit high radiation fluxes, like in SR experiments;
- the possibility of assembling large area systems, which is mainly determined by the space occupancy of the ASICs and by the possible disturb that one chip creates to the neighbors (mainly crosstalk and electromagnetic noise).

Current counting systems are able to discriminate photons of energy lower than 10 keV, with a counting speed higher than 1 MHz, however there is only one operating detector with a large number of channels [164].

There is a trend toward an energy characterization of the detected photons. When using polychromatic beams a spectroscopic capability could be used in order to better characterize the imaged sample, or in order to apply innovative techniques like dual energy imaging [59, 60, 61] and K-edge subtraction [62, 63]. The implementation of multiple thresholds can be useful also in
applications using monochromatic radiation in order to enhance the spatial resolution or the rate capabilities of the system.

Counting pixel systems are also rapidly developing, with the advantage of a reduced capacitance of the detection system [70, 166, 167].
4. FRONTRAD

The FRONTRAD experiment aims to upgrade the SYRMEP detection system in order to prove the feasibility of clinical digital SR mammography \[143\].

In the geometry used at the SYRMEP beam line, the duration of a mammographic exam is given by the time needed for each step of the acquisition times the number of vertical steps. The time slot for each step depends on the statistics required, the intensity of the incident beam, the organ thickness and the efficiency of the detector. Figure 4-1 shows the total duration of the examination as a function of the maximum electronics rate. It is represented by a band instead of a curve since it shows the duration of the exam for breasts of various thicknesses (from 2.5 to 6 cm when compressed). The minimum duration of the exam has been estimated requiring a statistics of 5000 photons per pixel \((100 \times 300 \, \mu m^2)\) using a monochromatic beam of the energy that minimizes the acquisition time for each breast thickness; 250 vertical steps are required in order to scan a 15 cm sample with a two 300 \(\mu m\) thick layers detector.

At low electronics rates the exam duration is limited by the maximum rate accepted by the electronics, while at high rates it is limited by the detected X-ray flux, which depends on the intensity of the beam, the detector efficiency and the absorption by the organ.

CASTOR is able to support an incident rate up to 10 kHz without considerable efficiency loss, so that the time duration of the exam would be of about 2 minutes. The goal of FRONTRAD is to develop a digital system able to work with the full intensity of the used synchrotron beam \[168\].

Fig. 4-1: Total duration of a mammographic examination for various breast thicknesses as a function of the maximum electronics rate, using a two layer FRONTRAD digital detection system. The two plots represent the two possible electron energies at which Elettra is operated.
A great improvement is needed in particular in order to enhance the rate capability of the readout electronics with respect to CASTOR.

In this chapter the new sensors and readout electronics developed the project will be described and the measurements acquired with the first prototypes will be presented.

4.1 THE SENSORS

The FRONTRAD silicon microstrip detectors have been manufactured by Hamamatsu (Japan) on high resistivity silicon wafers [169].

Seven different types of detectors were designed on the same set of masks, as shown in figure 4-2. All the detectors are 300 \( \mu \text{m} \) thick. The strip pitch can be 50 \( \mu \text{m} \) or 100 \( \mu \text{m} \), the strip length varies between 1 cm and 2.1 cm. The width ranges between a few centimeters (for detectors used for test purpose) and 13.5 cm.

Thanks to the high resistivity of the wafer (>4 k\( \Omega \)) and to the good quality of the fabrication processes, the leakage current results lower than 10 nA/cm\(^2\) in all wafers for bias voltages up to 100 V, as shown in figure 4-3a. Full depletion is reached at about 40 V, but the detectors are operated at 60 V in order to reduce the size of the undepleted region and increase the charge collection efficiency of the sensor.

The detectors have been designed in order to minimize the undepleted region in the entrance window of the sensors. For this purpose, they have a guard ring on only three sides, as shown in figure 4-4. The distance between the border of the detector and the bias ring ranges between 240 and 440 \( \mu \text{m} \). No significant difference in the detector leakage current has been measured in detectors with different cutting distances, as shown in figure 4-3b [11].

Figure 4-5 shows the efficiency of the FRONTRAD detectors as estimated from their geometric characteristics. It is represented by a band instead of a curve since it depends on the strip length and on the cutting distance, which are different for the various designs.

The detectors have been designed and fabricated in order to limit the sensor noise contribution to the overall ENC, as described in section 3.3. Figure 4-6 shows the various noise components as a function of the readout electronics peaking time \( T_{\text{peak}} \), as calculated in [120]. Since the ENC
Fig. 4-3: a) Average leakage current density of the FRONTRAD sensors and b) total leakage current for two detectors of type det4 with different cutting distance.

Fig. 4-4: Design of the detectors and picture in detail of a corner of the sensor. The guard ring is on only three sides.

Fig. 4-5: Efficiency of the FRONTRAD detectors.
due to the leakage current and to the polarization resistor is in parallel, it is proportional to the square root of $T_{peak}$, so that better noise performances can be obtained by reducing $T_{peak}$. On the other hand, the ENC due to the resistance of the metal strip is in series and consequently inversely proportional to $\sqrt{T_{peak}}$. Considering that this last component is much bigger than the other two, great care has to be taken in controlling the strip resistance in order to operate the detectors at high rates. Moreover, $\text{ENC}_{\text{metal}}$ is proportional to the strip capacitance $C_{\text{strip}}$, which also influences the readout electronics noise performances (equation 3.3).

$C_{\text{strip}}$ is mainly determined by the strip width, from which depend both the junction and the inter-strip capacitance. Figure 4-7 shows the total strip capacitance for detectors of 100 and 50 $\mu$m pitch. The interstrip capacitance has been approximated to that of two wires spaced as the strips (i.e. strip pitch minus width) [169]. $C_{\text{strip}}$ is proportional to the strip length, which in this case is up to 2 cm.

In order to limit the capacitance without compromising the charge collection efficiency of the detector, the strip width has been set to 2/3 of the strip pitch, so that $C_{\text{strip}}$ is of the order of 6 pF for 2 cm strip detectors.

The read out electronics is AC-coupled and the coupling capacitance are 70 pF for 50 $\mu$m and 160 pF for 100 $\mu$m strip pitch. In both cases the coupling capacitance is higher than 10 times $C_{\text{strip}}$, in order not to increase the detector capacitance. DC (Direct Coupling) pads are also present.

4.2 THE FRONTEND ELECTRONICS

In order to improve the rate capability of the detection system, a new photon counting ASIC called FROST has been designed by a collaboration between INFN (Istituto Nazionale di Fisica Nucleare) Trieste and Aurelia Microelettronica [168].

FROST is a mixed analog-digital ASIC consisting of 64 channels fabricated in VLSI (Very Large Scale of Integration) CMOS 0.8 $\mu$m technology (figure 4-8a). The channels are completely independent and they work in parallel during the acquisition phase, while their content is sent out serially during the read out.

Each channel consists of (figure 4-8b):
- a low noise folded cascode preamplifier with capacitive feedback with adjustable polarization voltage;
Fig. 4-7: Strip capacitance per cm as a function of the strip width for a) 100 µm and b) 50 µm strip pitch. The cases of strip with zero or equal to the strip pitch are obviously senseless.

Fig. 4-8: a) Picture of the ASIC FROST and b) layout of a channel.
- a CR-RC\(^2\) shaper with pole-zero cancellation;
- a discriminator with a variable threshold with Schmitt trigger and hysteresis; the threshold is composed of a part common to all channels generated by a 6 bit DAC (Digital to Analog Converter) and a part adjustable for each channel generated by a 3 bit DAC;
- an asynchronous 16 bit counter with serial readout in both directions and with a maximum readout speed of 140 MHz.

The shaper output of channel 0 is buffered and taken out for monitoring the working conditions of the ASIC analog section. A calibration input with a 200 pF internal test capacitor is provided. The digital section allows both an acquisition and a readout test mode and generates an overflow level if any of the channels count more than \(2^{16}-1\). The ASICs are designed in order to be daisy-chained.

### 4.3 Measurements

Several prototypes of the detection system of different size have been developed in order to evaluate the performances of the ASIC.

A schematic of the readout system used is shown in figure 4-9. Several multilayer printed circuit board have been designed by INFN Trieste and produced by Ilfa (Germany) in order to test

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**Fig. 4-10:** Picture of a) the FROST repeater and b) the VME 16 bit I/O register.
A PCB (Printed Circuit Board), called FROST repeater, has been developed in order to distribute the supplies and the signals to the ASIC PCB (figure 4-10a).

The timing signals are controlled by a PC (Personal Computer) and sent to the repeater through a VME (VERSA Module Eurocard) 16 bit I/O register (figure 4-10b) [170]. The acquisition program is written using the Tcl/Tk graphical interface and shared libraries implemented in C [147, 171]. The sample movement is controlled by micrometric motion stages addressed by GPIB (General Purpose Interface Bus) [172].

### Single ASIC system

The first measurements using FROST have been performed using a single ASIC in order to evaluate the main characteristics of this new readout electronics.

The detector used for the first tests is a silicon microstrip detector manufactured by SINTEF (Norway) with 50 µm strip pitch and 300 µm thickness. Each readout channel was bonded to two strips in order to obtain a pixel size of 100 µm. The dead zone in front of the strips is 0.9 mm, while the strip length is 1 cm. Ten guard rings keep the dark current very low (few nA) but the absorption efficiency of the detector results also quite low.

Figure 4-11 shows the picture of the single ASIC system. The ASIC absorbs a current of 140 mA and the power consumption is about 11 mW per channel.

Figure 4-12a shows the shape of the analog signal of FROST channel 0 using photons generated by an $^{241}$Am source. The peaking time is of about 240 ns and the signal ends within 1 µs. No significant undershoot is present.

In order to evaluate the noise of the electronics, the buffered analog output of channel 0 of the ASIC has been fed into an ADC LeCroy 3511. Figure 4-12b shows the spectrum of a $^{241}$Am source. By calculating the ratio between the 60 keV photon peak position and its FWHM, it is possible to evaluate the ASIC electronic noise, which results to be about 870 $e^-$, very close to the design requirements of 800 $e^-$. The signal had to be differentiated before being put into the ADC and this derivation step can easily explain the difference.

The ASIC has been tested using a HP33120A pulse generator in order to evaluate its gain and offset.

Figure 4-13a shows the 6 bit threshold scan for different 3 bit DAC values for a FROST channel for 1 fC pulses injected using the calibration input of the ASIC. The LSB (Least Significant Bit) value of the 3 bit DAC is the opposite of the angular coefficient of the line obtained by fitting the 3 bit DAC value and the threshold scan flex point position. The distribution of the 3 bit DAC LSB value has a 10% spread among the channels.

Stair pulses of different amplitude have been injected using the calibration inputs in order to
Fig. 4-12: a) FROST analog signal and b) spectrum of 60 keV photons from a $^{241}$Am source. The solid line fitting the photon peak is a gaussian whose parameters are shown.

measure the ASIC gain. The input charge has been evaluated using for the internal calibration capacitance the nominal value of 200 pF. Figure 4-13b shows threshold scans for different input charge values for a FROST channel. The gain is given by the angular coefficient of the line obtained by fitting the input charge versus the flex point position. The mean gain for the 64 FROST channels examined is about 125 mV/fC with a 4% spread, while the offset has a spread of only 2% after the 3 bit threshold has been adjusted.

Fig. 4-13: Threshold scan of one FROST channel of a) 1 fC pulses at different 3 bit threshold values and b) for input stair pulses of different amplitude. In both cases, an $erf$ function is fitted with the experimental points.
A fixed number of Poisson-distributed pulses has been injected at different rates in the calibration inputs in order to evaluate the ASIC behavior at high rates. Figure 4-14a shows the threshold scan curve as a function of rate. A loss of counted pulses is observed at high rates, due to the pile up phenomena described in section 3.4. The expected increase of counts for threshold higher than the pulse height is also observed. The ASIC efficiency can be calculated from the ratio between counted and injected pulses. The mean efficiency is shown in figure 4-14b and is very uniform on all the channels of the ASIC. The efficiency is 100% up to 50 kHz and remains higher than 90% up to 200 kHz, in agreement with the results of the simulation in figure 3-11a for timing settings close to the FROST specifications.

The single ASIC system has also been tested with SR at the SYRMEP beam line. The use of photons allows to obtain data without the possible signal distortions due to the pulse generator. However, the setup the the beamline is more noisy. The gain has been calculated by acquiring threshold scans with photons of different energies, considering that it takes about 3.6 eV to generate an e-h pair. The data are then fitted with an erf function and the energy linearity and gain of the ASIC are evaluated by fitting the charge produced and the flex points position with a straight line. The calculated mean gain is 120 mV/fC with a spread of about 5% on the channels, while the offset spread is just 2% after the fine threshold has been adjusted. The gain value is slightly lower than that measured in laboratory possibly due to a miscalibration of the input capacitance.

The high SR intensity allows to evaluate the rate response of the ASIC at very high rates. Figure 4-15a shows a threshold scan at 32 keV for different incident photon rates obtained by putting aluminum filters of various thickness between the monochromator and the detector. The threshold scan shape at high rates is very different from the erf function expected, and for rates higher than 1 MHz the number of counts results lower than at 700 kHz in the same time interval. The efficiency decreases at higher thresholds and this result can be due both to a baseline shift or to a high noise level, as discussed in section 3.4. The latter is probably the cause of the efficiency loss in the case of FROST, since negligible undershoot is observed in the analog signal.

Figure 4-15b shows the relationship between photons counted by the detection system and number of X-rays that impinges on each detector pixel. The incident flux is evaluated from the
Fig. 4-15: a) Threshold scans at 32 keV for different X-ray rates for a FROST channel and b) efficiency loss as a function of rate: the straight line interpolates the experimental points at low incident rates and shows the expected detected rate for 100% electronic efficiency.

Fig. 4-16: a) Mean FROST efficiency as a function of rate at different energies compared with CASTOR efficiency. b) Variance to mean ratio for the images background at different rates. The acquisition time is 0.1 s except where differently specified.
current measured by the ionization chamber. If the electronics efficiency were 100% at all rates, the points should lay on a straight line, whose angular coefficient is the silicon sensor efficiency \( \eta \). The sensor efficiency can be evaluated by fitting the experimental data at low rates (where the electronics efficiency is considered 100%) with a straight line. The measured \( \eta \) is close to the values evaluated from the geometric characteristics of the detector. This means that the discrimination between noise and signal is good enough to count all the photons impinging on the detector.

In order to evaluate the contribution to efficiency given by the electronics, it has been considered the ratio between the data and their projection on the straight line of figure 4-15b, which represents the photons absorbed by the detector. The mean efficiency is plotted in figure 4-16a for different energies. It results to be quite uniform on all the channels and is in good agreement with the efficiency measured in laboratory (figure 4-14b). The dependence of the efficiency from the photon energy is negligible, however there is a slight increase at 32 keV due to the higher SNR signal.

Figure 4-16b shows the ratio between the variance and the mean calculated for the background of the images taken at different rates. If the detection system followed the Poisson statistics this ratio should be 1. For low rates increases the acquisition time, and so the number of noise events, resulting in a variance higher than the mean. For rates higher than 300 kHz the electronics saturates and the variance results to be less than the mean. This behavior is compatible with the simulation, as shown in figure 3-12a.

The single ASIC system has also been used in order to acquire images of a C/D (Contrast/Detail) phantom (Gammex,RMI 180) for contrast resolution measurements at different rates, as shown in figure 4-17a. The phantom consists of plexiglas disks of different thicknesses, whose theoretical contrast can be calculated from equation 1:3 by using the attenuation coefficient of plexiglas.

Figure 4-17b shows the measured contrasts for the disks of the C/D phantom as a function of rate. There is no considerable loss of contrast up to 100 kHz. The solid lines in figure 4-17b are calculated from equation 2:12 using the mean efficiency of the ASIC at 22 keV from figure 4-16a.

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**Fig. 4-17:** a) Image of a column of disks of the C/D phantom acquired at 22 keV and 100 kHz and b) measured contrast for the disks of the contrast detail phantom as a function of the rate. The solid lines are calculated from equation 2:12 using the mean efficiency of the ASIC at 22 keV from figure 4-16a.
ii. The four ASICs system

The first multi-ASIC system is made of 4 FROSTs bonded to a 244 channels Hamamatsu detector (described in section 4.1) and is shown in figure 4-18.

Gain and efficiency measurements have been performed on the system and the results were completely compatible with the ones obtained for the single ASIC assembly.

Images of a C/D phantom have been acquired in order to measure the contrast resolution at different rates. The measured contrasts for the disks have been compared to the theoretical ones. The experimental points were close to the predictions and showed little correlation with the photon rate up to 200 kHz (figure 4-19). The faintest visible disk has a contrast of 0.6%.

Figure 4-20 shows an image of the Ackermann phantom (Gammex, RMI 160) [173] acquired at 25 keV and 80 kHz. The phantom contains mammographic details of decreasing size. The details of the first four series are visible. Since the acquisition time is not adjusted via a real time system, some lighter horizontal lines are visible, due to fluctuations in the timing of the acquisition.

![Figure 4-18: Picture of the 4 ASICs system.](image1)

![Figure 4-19: a) Image of a C/D phantom at 25 keV at 90 kHz and b) plot of the measured contrast for the 6 thickest disks at 25 keV as a function of rate.](image2)
system.

iii. The 10 cm ASICs assembly

A 16 ASICs system has been assembled, as shown in figure 4-21. The 1024 channels are bonded to a 12 cm long Hamamatsu detector with 100 µm strip pitch described in section 4.1. The width covered is 10 cm.

Test measurements have been performed on the system. The complicate structure of the PCB made the system quite noisy. The DAC current bias is shared between all the ASICs causing a malfunctioning of the system. The reference voltage of the DAC was very dishomogeneous on the various ASICs and the adjustment of the threshold on a channel by channel basis is not possible. The problems found can be probably solved with a redesign of the PCB.

The system has been tested at the SYRMEP beam line in order to acquire images of
mammographic phantoms.

Figure 4-22 shows an image of an Ackermann phantom obtained at 22 keV. The image quality is poor and the counts acquired by the ASICs are very inhomogeneous. These problems are probably due to the malfunctioning of the PCB. Since the system was very noisy, a very high threshold has been kept resulting in a low counting rate and in a normalized image not properly corrected for disuniformities between channels.

4.4 PERSPECTIVES

The measured characteristics of FROST correspond to the specifications and are synthesized in the following table:
The good rate response of FROST should allow the acquisition of an entire examination at counting rates higher than 100 kHz. The duration would then be less than 10 s, as shown in figure 4-1.

However, the ASIC still presents some critical points for what concerns the noise performances. The problem becomes more important when many ASICs are operated together and the noise due to neighboring channels and to perturbations of the power supply create a disturb.

Moreover, the pad pitch of the ASIC is 140 µm and pads are present on all the sides of the die. This means that, for a strip pitch of 100 µm, a width almost double than that of the sensor is needed in order to place the ASICs. The limitation becomes stronger when using a smaller strip pitch of the detector. For example for 50 µm strip pitch the space needed for the electronics is four times the width of the sensor.

The problem becomes important for systems with many ASICs since the distribution of the signals and power supplies becomes problematic and the high parasitic capacitance of the fan-in to the detector can determine cross-talk effects and signal loss [174].

Although an improvement of the performances of the system could certainly be obtained by modifying the design of the PCBs, new difficulties would certainly come out from the need of assembling of a still greater system of 20 cm, which is the size required for mammography. For this reason new solutions for what concerns the read out electronics have been investigated.
5. MATISSE

The MATISSE experiment aims to develop a photon counting system for SR breast tomography. In this chapter the principles that allow tomographic reconstruction will be presented and the promising studies about the application of SR CT (Computed Tomography) to breast imaging will be discussed. The MATISSE detection system will be described in detail and the first measurements performed with prototypes will be shown.

5.1 BREAST COMPUTED TOMOGRAPHY

The Nobel prize for Medicine in 1979 was awarded to A. M. Cormack and G. N. Hounsfield because their work in the development of computed tomography “ushered medicine into the space age” [175]. Though neither of the laureates had a medical background, their work received immediate acceptance from the medical community thanks to the clear images of cross-sectional views of the human body that can be produced with this technique.

The main advantages of the computed tomography technique with respect to planar X-ray imaging are:

- Absence of superimposition of structures;
- Depth resolution;
- Contrast enhancement of soft tissues;
- Indication on absolute values for variations in tissue density.

The first three advantages are common also to tomosynthesis, which is the other main technique for obtaining three dimensional images.

After illustrating the principles for image reconstruction for both tomosynthesis and CT, their applications to breast imaging will be highlighted. The attention will then be focused on the results obtained with breast tomography with synchrotron radiation.

i. Digital tomosynthesis

If the image receptor and the X-ray generator are moved linearly in opposite directions, objects above and below the fulcrum are blurred proportional to their distance from their plane of focus, whereas the objects in the focal plane appear stationary [176]. The resulting image exhibit clearly the objects in the plane of interest, with anatomy from distant planes not visible because of blurring. The geometry of the acquisition is shown in figure 5-1a. In some cases the X-ray tube or both the X-ray tube and the image receptor are rotated around a center of motion. In this case some transform must be done to reduce the data to the case of parallel motion.

Before applying any reconstruction algorithm, a logarithmic transform must be performed on the acquired data. The resulting image is then linearly related to the attenuation of the sample (equation 1:1) and it is possible not only to render the structures in the focus plane (which could be done also with non linear data), but also to remove the blurring of superimposed anatomy.

The main reconstruction algorithm used in tomosynthesis consists in shifting and adding the
image obtained over the different projections, as shown in figure 5-1b. The structures present in the plane of interest are brought in coincidence while the superimposed objects are smeared out. However, the contrast of the object in the focal plane is lowered due the blurred structures, so that deblurring algorithms are required. For this reason, significant advances in this technique have been achieved only with the diffusion of digital image receptors and advances in computing.

Tomosynthesis has been applied to many clinical tasks, among which angiography [178], dental applications [179], chest imaging [180], imaging of joints in orthopedic [181] and mammography [182].

ii. Computed tomography

The fundamental concept underlying the technique of computed tomography is the capability of reconstructing or synthesizing a cross-section of the internal structure of a sample from multiple projections of a beam of radiation passing through the object [183, 184]. The technique is not limited to transverse sections, since cross-sections in other planes can be synthesized by secondary reconstruction using transverse cross sectional data.

A projection consists of the detected transmission values with the detector and radiation source oriented in the same direction, as shown in figure 5-2a. The image given by a set of such projections is called sinogram (figure 5-2b) [29].
The reconstruction of the tomographic image is usually achieved by analytical or iterative algorithms [185].

Iterative techniques are based on the principle of successive approximations: the value of the attenuation coefficient for each voxel is iteratively corrected so that the projection set acquired is best approximated. These techniques are usually employed in the reconstruction of single photon and positron emission computed tomographies (SPECT, PET) where the statistics acquired is very low and the noise contribution too high in order to reconstruct the cross-sections analytically.

The most used analytical method for tomographic image reconstruction is usually referred to as filtered back-projection method [186]. It dates back the work of the Austrian mathematician J. Radon, that in 1917 demonstrated that a three dimensional object could be replicated from the infinite set of all its projections [187].

Figure 5-3 shows the conceptual view of the problem. The Radon transform $p_\theta(t)$ is defined as the line integral of the function $f(x, y)$ at a given angle $\theta$:

$$p_\theta(t) = \int_{-\infty}^{+\infty} f(t \cos \theta - s \sin \theta, t \sin \theta + s \cos \theta) ds \quad (5:1)$$

In X-ray computed tomography, the goal is to map the attenuation coefficients of the sample starting from a sinogram acquired at discrete steps. From equation 1:1 one can see that the logarithm of a projection is the Radon transform of $\mu$.

The Radon inverse problem (i.e. the reconstructions of an object from multiple projections) can be solved thanks to the Fourier central slice theorem, which relates the two dimensional Fourier transform $F(v_x, v_y)$ of $f(x, y)$ with the 1D Fourier transform $P_\theta(v)$ of $p_\theta(t)$:

$$P_\theta(v) = F(v \cos \theta, v \sin \theta) \quad (5:2)$$
With enough projections $p_\theta$, one can thus calculate $P_\theta$ filling the Fourier space. By changing coordinate system from $(\nu, \theta)$ to $(\nu_x, \nu_y)$, $f(x, y)$ can be obtained as Fourier anti-transformed of $F(\nu_x, \nu_y)$:

\[
f(x, y) = \int_{-\infty}^{+\infty} \int_{-\infty}^{+\infty} F(\nu_x, \nu_y) e^{-2\pi i \nu_x x} e^{-2\pi i \nu_y y} d\nu_x d\nu_y = \int_{-\pi}^{+\pi} \int_{-\infty}^{+\infty} P_\theta(\nu) e^{-2\pi i \nu (x \cos \theta + y \sin \theta)} |\nu| d\nu d\theta
\]

One can define the filter function $b(t)$ as the Fourier antitransformed of $|\nu|$ and one can write:

\[
f(x, y) = \int_{0}^{\pi} \tilde{p}_\theta(x \cos \theta + y \sin \theta) d\theta
\]

where $\tilde{p}_\theta = p_\theta * b$ is the convolution between the Radon transform of $f$ and the filter $b$.

In clinical practice, the Radon transform of $\mu$ is sampled on the $t$ axis and the number of projections is finite, thus the Fourier transforms must be calculated in discrete steps (i.e. sums instead of integrals). One can only obtain an approximated solution and different filters can be used in order to improve the image quality [186].

The choice of the right filter for image reconstruction is of paramount importance in order to enhance the desired details. The weight assigned to frequencies close to the Nyquist frequency is particularly critical, since these spatial frequencies introduce statistical noise in the image. Filters that assign different weights to high and low frequencies can be used. In particular a high-pass spatial filtering enhances the edges but also increases the noise in the images, so it is often used for the imaging of high contrast areas (e.g. bones), where noise does not interfere with interpretation. On the other hand, filters that reduce the weight of high spatial frequencies are preferable for examining low contrast areas (e.g. brain, abdomen). Commonly used filter functions are the Hamming and the Shepp-Logan filters [186].

The tomographic reconstruction is a very critical task and artifacts in the image can arise if the acquisition or the reconstruction are not carried on properly. The reason for some of the most common artifacts are:

- An insufficient angular sampling, that can lead to the presence of artifacts in proximity of sharp intensity changes.
- Insufficient rotation amplitude that results in an undersampling of the reciprocal space $(\nu_x, \nu_y)$. The overall rotation angle must be at least $180^\circ$, but $360^\circ$ are used if the X-rays are divergent and some geometric transform must be applied in order to fill the Fourier space.
- Presence of very high absorbing details (e.g. metal) that absorb completely the radiation and lead to missing data in their shadow.
- Artifacts due to the patient motion, such as respiration and heart beat during data acquisition.
- High noise level, that can be compensated with a higher dose given to the patient in order to increase the visibility of structures.
- Finite resolution of the detector, that leads to the so called partial volume effect: a nonlinear response is obtained when the object structure or edge occupies only part of the X-ray beam measured by a single detector element. This results in streak artifacts that occur tangential to high contrast objects. Artifacts connecting details that occupy only part of the slice thickness can arise.
- Beam hardening when using polychromatic radiation since the low energy components are absorbed more than the high energy ones and thus the reconstructed attenuation coefficient of the sample results dependent on its thickness. Beam hardening artifacts appear as cupping, or a reduction of the reconstructed attenuation coefficient toward the center of a large object.
iii. Three dimensional breast imaging

Despite its high cancer detection accuracy, the capability of X-ray mammography is limited by its two-dimensional representation of a natural three dimensional entity \[12\]. Since breast contains overlying dense fibroglandular tissues, a deterioration of the contrast of the lesions is given by the superimposition of structures, particularly when dense breasts are imaged. Consequently, a small carcinoma of few millimeters in size is difficult to detect, resulting in a high false-positive rate \[98\].

A better diagnostic accuracy could be achieved with the use of 3D techniques, such as digital tomosynthesis and computed tomography. By slicing the breast volume into two dimensional images, the interior of the breast can be scrutinized and quantitatively analyzed using conventional 2D image processing techniques.

Moreover, the possibility of mapping the effective attenuation coefficients of the tissues allows a simpler application of texture characterization. An enhanced contrast and an improved detection of the edge shape can help a better discrimination between benign and malignant lesions. Three-dimensional breast imaging opens up new perspectives in volume representation, which as a result simplifies constituent analysis and spatial measurements.

The potential clinical benefits are a reduced recall rates and a better diagnostic accuracy that could avoid useless biopsies, while still improving the cancer detection capability particularly in women with heterogeneously dense breast \[12\]. Since compression is not needed, the examination can be better tolerated by women that are particularly sensitive to the unease of compression. Moreover, the depth information obtained from tomographic images can be useful for performing biopsies and selective surgery. The overall final result would certainly be a better tumor detectability.

iv. Breast computed tomography scanners

The shortcomings of planar X-ray mammography have partially been overcome by stereopsis 3D reconstruction from two or more views or by tomosynthesis.

Digital tomosynthesis systems for breast imaging have been developed \[177\]. Typically, the tube is rotated around $\pm 15^\circ$ and 7 to 12 exposures are obtained during a total scan of about 10 s, with the same dose of a planar mammogram. In modern digital tomosynthesis systems, the images are reconstructed with a slice separation of 1-2 mm, so that about 50 reconstructed slices can be obtained for each study. Rapid reconstruction time is essential and the post-acquisition processing should be kept to less than 30 s. The detector is usually given by a flat panel (see section 2.5).

Since the images are presented with reduced tissue overlap, objects are visualized with improved clarity leading to faster and more confident readings of the images.

However, a volume CT reconstruction can provide a more faithful and quantitative 3D representation in terms of X-ray attenuation coefficient. In the mid 1970s, a CT system specifically designed for fan-beam computed tomographic mammography was built and a clinical trial was conducted. The setup of the system is shown in figure 5-4a: the detector and X-ray source are rotated around the sample. A translation of the sample is needed in order to acquire more than one slice. The data suggested that breast tomography can differentiate potentially precancerous lesions from benign fibrocystic disease, especially if coupled to the use of a contrast agent \[188\]. However the technique was not considered suitable for screening of asymptomatic women because of the high dose given to the patient and the long scanning time that lead to motion artifacts. A large slice thickness and poor spatial resolution made difficult the detectability of small lesions.

CT scanners have evolved a lot and in recent years the development of dedicated systems for breast imaging is becoming popular. In order to reduce the scanning time, two kinds of setup are mainly applied:

- Multi-detector CT scanners can acquire multiple data sets with each rotation of the X-
a) Fan-beam setup  
b) Cone-beam setup

Fig. 5-4: Tomographic setup in a) fan-beam and b) cone-beam geometry

Ray tube and can scan through large anatomic areas three to seven times faster than can single-detector fan-beam CT scanners. The high speed and the thin collimation of the beam improve the spatial and time resolution of the images acquired [189]. Recent studies prove that the technique is superior to mammography and sonography in the depiction of the margins of the tumor invasion [190].

Cone-beam CT is based on full field digital detectors, mainly flat panels (see section 2.5), which have now a high spatial resolution and a high frame rate which allow real time image grabbing [98]. The patient lays in prone position with the organ dangling and the breast is completely illuminated by the cone beam. Detector and X-ray source rotate, as shown in figure 5-4b. The reconstruction algorithms are more complex than in the fan-beam case and they introduce approximations and noise in the reconstructed image. However, the acquisition is very fast and the system can provide significantly better low-contrast detectability of tumor masses and a more accurate localization and volume visualization of the lesion with respect to planar imaging [12, 64, 129, 191, 192].

Since the breast is uncompressed, higher X-ray energies are employed. X-ray tubes with tungsten anode and 80-120 kVp have been used. This allows to limit the dose of radiation: for thin breasts, the radiation level results almost double than in planar mammography, but for dense breasts the dose can be kept at the same level as in a conventional mammogram [64].

These techniques still have some limitations concerning spatial resolution and dose, but these problems will probably disappear as the hardware (i.e. CT scanner) and software (i.e. reconstruction algorithms) improve [12].

v. Synchrotron radiation breast computed tomography

Synchrotron radiation experiments represent a further step forward with respect to conventional X-ray tubes:

- The laminar beam allows the removal of scattered radiation, thus increasing the image quality.
- The negligible divergence of the beam allows the use of reconstruction algorithms simpler than in the fan-beam case, thus introducing less approximations and noise in the image. Moreover, the rotation can be performed on only 180°.
- The possibility of selecting the most suitable energy for each clinical case according to the organ thickness and composition, allows a significant reduction in the delivered dose [193]. Furthermore, the use of monochromatic beams removes beam hardening artifacts, which result in decreased contrast and poor quantitative analysis capability when typical mammographic spectra are used [194].
A more accurate tissue characterization is possible thanks to the possibility of recovering the map of the absolute attenuation coefficients of tissues, instead of the effective ones as in the polychromatic case.

In SR tomography, since the beam is stationary, the sample will rotate. The rotating object is ideally divided into slices parallel to the beam plane. If the rotation axis is not orthogonal to the beam, a detail will move into contiguous slices during a rotation. The detail contrast will thus be spread across several slices. An alignment better than $0.05^\circ$ is required in order to avoid the presence of artifacts in the reconstructed image [193].

Figure 5-5 shows the image of a breast sample acquired at the conventional mammographic station at the hospital in Trieste and a tomographic slice of the same sample acquired at the SYRMEP beamline [13]. In the planar mammography case, the visibility of the anatomic patterns is strongly limited by the superimposition of the structures. The geometry of figure 5-5a is not representative of a conventional mammogram, but it is used in order to compare the image with the tomography in figure 5-5b. The improvement in the visualization of structures in the tomographic image is very strong and a volume segmentation can be applied. The dose given to the sample is 1.6 mGy.

The results show the possibility of using breast CT as a second-examination tool, providing further information with respect to conventional mammography, and delivering a dose comparable to that delivered in clinical mammography [13, 65, 193, 195].

Diffraction based tomographic characterization of breast tissues has shown an optimum correlation between the structures detected in the images and the results obtained in histology [52]. However, the dose used in the acquisition is still much higher than in planar examinations. A strong dose reduction can certainly come out from a compromise on the image quality.

DEI-CT images show the pure image of the out-of-plane gradient of the X-ray index of refraction with no artifacts [196]. Yet, CT exploiting phase effects still presents some critical points in image reconstruction [197]. The application of the standard filtered backprojection algorithm, in fact, allows only qualitative reconstruction, allowing one to obtain the location of the boundaries of the regions with different refraction index with poor quantitative information.
The problem can be solved by a two step approach, first retrieving the radon transform of the phase information and then applying the backprojection algorithm \cite{198}, or by implementing a complete mathematical theory that can relate the phase function and the projection data \cite{197}.

\textit{vi. Detector requirements}

The tomographic examination differs from mammography and imposes then different requirements on the detection system. In particular:

- The breast is uncompressed and the examination is performed at higher energies. A high efficiency is thus required in the 25-32 keV energy range;
- Only a few hundreds photons must be acquired in each projection in order to keep low the dose of the examination. For this reason, the detector noise should be negligible in order to obtain an high image quality.

The first requirement is satisfied by \textit{edge on} silicon detectors (see section 3.2). The detector efficiency results still higher in the tomographic than in the mammographic energy range, as shown in figure 3-3b. The spatial resolution obtained with a 100 μm pitch microstrip detector and a parallel radiation beam is better than what can be obtained for examples with flat panels in cone-beam geometry since both the PSF of the flat panel coupled to the phosphor screen usually have a FWHM of few hundreds microns and the X-ray geometry introduces blurring in the image reconstruction.

By avoiding the presence of reset and read out noise, photon counting allows to minimize the fluctuations on the number of detected photons (see section 2.4). The difference between the counting and integrating read out is particularly strong when a small number of photons is detected, as shown in figure 2-6. Since the photon energy is higher, the noise requirements on the electronic chain are slightly less stringent.

In order to reconstruct the image, the whole organ must lay in the field of view of the detector. Both the sensor and the read out ASIC should then be feasible for assembling large systems.

5.2 \textbf{THE MATISSE DETECTION SYSTEM}

For the reasons highlighted in the previous paragraph, the \textit{MATISSE} detection system, optimized for SR breast tomography, is based on a silicon microstrip detector with application specific read out electronics operating in single photon counting mode. A sketch of the detection system is shown in figure 5-6.

The detector requires a width of at least 20 cm. Since the maximum sensor width available is 13 cm, it will be made out of two layers, each consisting in two detectors tiled on the side parallel to the strips. The insensitive region between the two sensors will be misaligned one layer from the other, so that the full set of data needed for the image reconstruction will be available if the data from the two planes are summed up.

The thickness of the tomographic slice will then be given by the detector thickness and will be of approximately 700 μm. When performing multi-slice acquisition, the slice thickness can be reduced by scanning the sample with vertical steps smaller than the detector thickness. An helical sample movement has also been applied with acceptable results for what concerns the image reconstruction \cite{199}. If only one slice is imaged, another way for reducing its thickness is the use of a thin beam illuminating only partially both the layers. In this case, if not shielded by means of a slit, the undetected radiation in the region between the layers would have a higher weight in the dose calculation.

Since the pixel size is 100 μm, more than 2000 channels will be present on each layer.

The detector will be completely integrated in the examination control system, and will have to satisfy strict safety rules needed in order to perform examinations on patients.
The silicon sensors have been largely described in section 4.1. In the following, the photon counting frontend electronics and the FPGA (Field Programmable Gate Array) based DAQ (Data AcQuisition) will be presented.

### The frontend electronics

The requirements of SR tomography concerning the read out electronics are fulfilled by the va64_tap and ls64 ASICs by IDEAS ASA (Norway), fabricated in 0.8 µm CMOS technology [200, 201]. The va64_tap has been originally designed for the readout of the hybrid photodiodes of the ring imaging Cherenkov detector of the BTEV experiment at Fermilab (USA) [202].

The va64_tap ENC specification is 500 e⁻ with a detector capacitance of 10 pF, that should allow a SNR(signal) of 10.

The layout of a channel is shown in figure 5-7. The preamplifier together with the selectable gain-stage can reach a gain of 100 mV/fC. The output is filtered by a CR-RC fast shaper with a peaking time of 75ns. Each channel has a discriminator, with a 4-bit DAC to reduce threshold spread. The ASIC has 64 parallel trigger outputs (one per channel) encoded as a current, and should be terminated with low impedance.

A trig_out signal is given as the wired-or of the outputs of all the channels and can be enabled by the digital configuration register of the va64_tap.

The gain and shaping of the signal and the time duration of the output logic signals can be tuned by means of external analog signals.

The outputs of the va64_tap are directly bonded to the ls64 ASIC, as shown in figure 5-8.
The $ls64$ works as 64 parallel level shifters, converting the logic signals from a current open drain logic into LVTTL (Low Voltage Transistor-Transistor Logic) CMOS levels (i.e. 0-3.3 V). The $ls64$ should minimize the coupling between the digital circuitry and the noise sensitive analog chip.

The parallel digital outputs are then fed into a PLD (Programmable Logic Device) that carries out the counting and read out functions.

**ii. The data acquisition**

Figure 5-9 shows the blocks that control the detection system. The acquisition can be divided in three main blocks, that also correspond to three different components:

- The $va64$ tap configuration register allows to select the activation of the gain stage, the selection of the threshold polarity and the enabling of the global trigger output and of a circuitry for the compensation of the detector leakage current \[200\]. It is also possible to enable a single-channel test modality, disable some channels and adjust the 4-bit fine
threshold on a channel by channel basis. The configuration string is written serially and the
register provides a serial output in order to daisy chain the ASICs.
◦ A digital potentiometer allows one to set the global threshold value. An incremental DAC
has been used [203].
◦ A FPGA that performs all the main functions for the control of the acquisition systems. The
FPGA functionality has been implemented by means of VHDL (Very high speed integrated
circuit Hardware Description Language) programming [204, 205] and can be further divided
in sub-blocks:
 ◦ A configuration register, that allows to select the acquisition time $\Delta t$ by serially
introducing the binary string corresponding the the number of timing clock counts
given in the time slot. The timing clock is obtained by means of a 4 MHz quartz
oscillator.
 ◦ A timer, that counts the timing clock pulses and enables the acquisition for a time equal
to the value set in the configuration register. When $\Delta t$ has passed, the timer disables
the counters and produces a LAM (Look At Me) signal.
 ◦ A 16-bit counter implemented for each channel. The counter is reset at the beginning
of each acquisition and the acquisition is enabled by the timer. The counter input
pulses are the detector outputs or, in case the test modality is enabled, a digital signal
common to all channels. Whenever one of the counters reaches the maximum value
(in this case $2^{16} - 1$) an overflow signal is generated.
 ◦ A loadable shift register for the serial read out of the counters. After the shift register
is loaded, the timer and counters are reset.
In order to implement the shift register more efficiently, it is subdivided in 16-bit shift
registers (one per channel) that are enabled one at a time. Thanks to this solution it is
possible to operate large shift registers, that would not work otherwise because of the
propagation delay of the shift-clock signal.

Figure 5-10 shows the flowchart of the acquisition. With this architecture the counting and
readout operations can be performed simultaneously and the acquisition can be stopped in
every moment. The process on the left is completely controlled by the user, while the one
on the right is executed in background by the FPGA.
Since the FPGA is completely configured via software, it can be modified with the only
restrictions given by the device connections.
The devices chosen are APEX 20K by Altera [206]. The gate density and pin-out depend
on the size of the prototypes assembled.

5.3 MEASUREMENTS

The printed circuit board shown in figure 5-11a (MATISSE repeater) has been developed in order
to distribute the power supplies and the logic signals to the ASICs and FPGA. On the PCB are
also mounted the quartz oscillator that generates the timing clock signal, the DAC for the ASIC
global threshold settings and an EPROM (Erasable Programmable Read Only Memory), i.e. a
configuration device that downloads the read out implementation on the FPGA every time the
power is turned on [207]. The EPROM can be reconfigured with the appropriate software by means
of a JTAG connector mounted on the repeater. Since every configuration device can program up
to 8 identical FPGAs at a time, the repeater can be used to control multi-ASIC and multi-FPGA
systems.

All the acquisition is controlled with the VME 16-bit I/O register of figure 4-10b and the
experimental setup is almost the same of figure 4-9 [170].
Moreover the possibility of remotely controlling the electronics and detector power supply, the
pulse generator and the oscilloscope via GPIB bus has been added [172].
Fig. 5-10: Flowchart of the acquisition of the MATISSE detection system.

Fig. 5-11: a) Picture of the MATISSE repeater and b) sketch of the detector alignment system.
Since the alignment of the detection system with the beam plane is a critical task, a micrometric positioning system has been designed. It is made of a vertical movement stage, two goniometers and a rotation stage, as shown in figure 5-11b, and can be remotely controlled with the serial RS-232 interface. Thanks to its small size, the alignment system can be positioned on the rails behind the patient support of the mammographic station at SYRMEP.

The acquisition program has been written in C and the GTk library has been used for the graphical user interface [146, 147].

The single ASIC system

A single ASIC multilayer PCB has been designed for test purposes and is shown in figure 5-12. For this first prototype, the MATISSE repeater had not been designed yet, and a general purpose PCB was used to distribute the power supplies. For this reason, the EPROM, the voltage regulators and most passive components are placed on the detector PCB itself. No DAC for threshold adjustment is present, so that the threshold must be changed manually by means of a potentiometer.

Pulses of various frequencies have been injected through the va64 Jap analog inputs in order to test the ASIC efficiency response at high frequencies. The counted pulses linearity was optimum and no efficiency loss was observed for pulse rates up to 3.5 MHz, as shown in figure 5-13a. This high rate should allow to perform an examination exploiting the whole synchrotron radiation flux.

The prototype was also tested in order to detect photons from a $^{241}$Am radioactive source. The profile of the source placed in the center of the detector is shown in figure 5-13b for several threshold values.

The gaussian profile of the source is clearly visible although the data were not normalized for threshold value dishomogeneity. A plateau is not completely reached for intermediate threshold values because of the presence of a charge sharing effect between neighboring channels (5-10%) [105].

Images of a mammographic test object have been acquired at the SYRMEP beam line at Elettra. Figures 5-14a and 5-14b show the images of a column of the C/D phantom acquired at 28 and 32 keV respectively. The two energies were chosen because they are suitable for CT examinations of thick breasts, which are performed at energies higher than planar mammographies.
Fig. 5-13: a) Rate response of the detection system using pulses injected in the va64 tap inputs and b) threshold scan performed by using a $^{241}$Am source.

Figure 5-14c shows the measured contrasts for the disks, which result close to the theoretical ones at both energies. The faintest visible disks have a contrast lower than 1% with a statistic of about 10000 counts/pixel.

ii. The six ASICs assembly

A new printed circuit board containing six ASICs (384 channels) was designed and connected to a silicon sensor. The sensitive width is 3.84 cm (figure 5-15). This circuit is a good candidate to

Fig. 5-14: Image of a C/D phantom acquired at a) 28 keV and b) 32 keV and c) comparison between the measured and theoretical contrast of the disks.
become the module that will constitute the final detector by means of replication of this scheme up to reach the desired dimensions.

Some preliminary tests were performed with the prototype. After acquiring images of high contrast objects using an X-ray tube with molybdenum anode, the system has been tested at the SYRMEP beam line.

Figure 5-16a shows the image of some of the simulated tissues of the Ackerman phantom [173] acquired at 25 keV.

The figure 5-16b shows the image of the C/D phantom obtained at 20 keV. The measured contrasts are comparable with the ones that can be calculated from the attenuation coefficient of plexiglas.

However, the disuniformities between channels are strong and many channels do not work properly. A further optimization of the ASIC’s parameters has to be done in order to improve the performances of the detector for reaching the characteristics of low noise and high speed requested by the project.

5.4 FUTURE WORK

The first results obtained with the MATISSE detection system are encouraging for what concerns the rate response and the noise capability, however some work is still needed in order to optimize the performances of the last prototype.

As soon as the problems with the current 3.84 cm prototype will be solved, the work will be directed toward the development of the large detection system sketched in figure 5-6. The next milestones are:

Fig. 5-16: Image of a) simulated tissues of the Ackermann phantom acquired at 25 keV and b) a C/D phantom acquired at 20 keV.
All the ASICs need to be electrically and functionally tested before being mounted on the PCB. Since the yield loss of the ASIC production is about 10%, almost 20% of the va64_tap-\textit{ls64} pairs should be replaced i.e. more than 10 ASIC pairs in the final detection system. This would increase the assembling time and costs, thus a test system has been developed. The two probecards (one per ASIC type) shown in figure 5-17 have been designed and produced by Technoprobe (Italy). The PCBs have been designed with particular care in order to limit the noise. The probe density is very high since the minimum distance between the pads of the ASIC is 80 $\mu$m. A program that allows an automatic test of the ASICs has been written in C with GTK graphical interface. The defined test protocol is going to: (i) measure the power consumption of the ASIC; (ii) scan the configuration register of the va64_tap; (iii) perform a threshold scan for each channel with pulses injected in the calibration pad or in each channel input. The tests will possibly give interesting informations also concerning the ASIC’s optimal operation parameters.

The 2000 channels detection will be designed with great care for what concerns the noise performances. Three prototypes will be assembled and the two with the best performances will be chosen and mounted back-to-back in order to build the two layer system. For this reason particular attention has to be taken in order to satisfy the mechanical requirements of the final assembly.

A new DAQ system will be implemented. Due to the large data amount that has to be transferred for each acquisition step (2000 channels $\times$ 16 bit), the time needed for serial read out would result much larger than the counting time slot, leading to a non negligible dead time in the acquisition. A custom VME board with larger data input connector (at least 64 bit) and a memory capable of store all the data of a complete examination will be implemented. With these configuration the data will be rapidly transferred from the FPGA on the detector PCB to the DAQ board, with a clock given by a quartz oscillator of several MHz and a large data transfer bus, and then collected by the user with the time delays due to the 16-bit data bus and clock speed of the VME interface used.

The detector will be integrated in the SYRMEP beamline for clinical mammography. This means that the detection system will be able to communicate with the control and safety systems of the mammographic station. In particular, it will generate an emergency stop signal in case that some danger situation is detected and will be able to control the shutters and patient support movement.

The final MATISSE detection system should be delivered at the end of 2005. It is intended
to be the prototype from which to start the engineering of a detector for tomographic clinical examinations.
CONCLUSIONS

This thesis describes the work on the development of detection systems optimized for breast imaging.

Breast cancer is the most common tumor and the second cause of death for women living in the industrialized countries \([2]\). The key to surviving breast cancer is early detection and treatment. According to the American Cancer Society, when breast cancer is confined to the breast, the five-year survival rate is close to 100%. The early detection of breast cancer helps to reduce the need for therapeutic treatment and minimizes pain and suffering, allowing women to continue leading happy, productive lives.

A high-quality mammogram is the most effective examination for screening the general population to detect breast cancer at early and treatable stages. However, mammography has some limitations: as many as 17% of cancers go undetected and the risk of a false-positive resulting from a screening mammogram is higher than 10%. Research suggests that, among women who receive annual mammograms for 10 years, half will have at least one suspicious finding leading to additional tests showing it to be a false alarm. Dense breasts are particularly critical since masses and microcalcifications are easily occult in the overlying glandular tissue.

Besides its limitations and drawbacks, mammography holds the greatest potential to save lives over other new screening and detection technologies, at least in the immediate future. Improvements in the mammographic examination can come from advances in the radiation characteristics and in the detection capability, connected mainly to the development of innovative X-ray sources and digital detection systems. These upturns can also lead to the exploitation of new imaging techniques that can broaden the diagnostic power of X-ray breast imaging.

A monochromatic X-ray beam of tunable energy allows one to maximize the image quality to dose relationship, since the soft X-rays of a polychromatic spectrum are not present \([5]\). In the first chapter it has been shown that a high intensity radiation beam produced by a synchrotron radiation machine can be monochromized still obtaining a radiation flux intense enough in order to perform clinical examinations \([24]\). Moreover, the synchrotron radiation beam is coherent and allows thus the observation of the phase alterations of the radiation traversing a sample by detecting the scattered photons or the interference between the diffracted and undiffracted wave \([40]\). Several medical tasks exploiting both absorption and phase contrast effects have been implemented at SR facilities world-wide in order both to optimize imaging techniques that can successively be exploited in hospitals and for performing SR examinations \([18]\).

Currently the only synchrotron radiation project with perspectives of clinical application in the near future is the mammographic facility which is being built at Elettra, the Trieste SR source \([7]\). The SYRMEP (SYnchrotron Radiation for MEdical Physics) beamline has been deeply modified in order to allow perform clinical mammographic examinations and is now expecting the necessary authorizations in order to start its activity. Although the accessibility of synchrotron radiation facilities is poor, SR presents such characteristics that are not achieved by any other X-ray source. The mammographic facility is obviously not built for screening purposes, but in order to examine women that present a particularly dense breast or have a high risk of contracting breast cancer (e.g. familiarity, previous tumor).

In the first phase, the examinations will be performed using conventional screen-film system
in both absorption and phase contrast modality, but the goal is to move toward digital and, finally, tomographic imaging.

Digital mammography systems are greatly improving and slowly becoming available in most hospitals. Studies comparing conventional and digital mammography have shown that digital detectors perform with the same or better results with respect to screen-film systems in terms of detecting breast cancer. In the near future, digital mammography may provide many benefits over standard film mammography, mainly by improving the contrast between dense and non-dense breast tissue, by providing easier image storage, by allowing the physician to manipulate breast images for more accurate detection of cancer, by preventing the problem of over-exposure avoiding thus the repetition of mammograms and by permitting transmission of images for remote consultation [57]. The main disadvantage of digital mammography systems is the initial cost, which is partially compensated by avoiding the expenses of film material and development and by strongly reducing the cost for image storage. Some of the commercially available digital mammography detectors have been presented in Chapter 2.

The detection systems developed in this work rely on a direct conversion sensor and a counting read out, as discussed in Chapter 3. Silicon microstrip detectors oriented with the strips parallel to the impinging beam provide a high detection efficiency for X-rays in the mammographic energy range, since the absorption depth is given by the strip length [9]. The pixel size is determined by the strip pitch and by the wafer thickness and, with a strip pitch of 100 µm, the spatial resolution is improved with respect to phosphor based clinical digital systems of at least a factor two. The high sensitivity of silicon allows one to perform the read out by counting single photons. Photon counting detectors allow the maximization of the visibility of the details in the image [10]. However the development of counting frontend electronics still presents some critical points, mainly the noise level, in order to detect low energy X-rays, and the speed of the electronic chain, for the exploitation of high radiation fluxes as in synchrotron radiation experiments.

In Chapter 4, the detection system developed for the FRONTRAD experiment has been described. New silicon sensors with a high efficiency and a low leakage current have been designed and fabricated [11]. The system is optimized for synchrotron radiation mammographic examinations and the frontend electronics improvements are directed toward an enhancement of the speed of the electronics. The ASIC developed for the experiment has demonstrated no efficiency loss up to 100 kHz counting rate, so that the duration of a synchrotron radiation examination is shorter than 10 s. The main limitations of the ASIC concern the non negligible noise and the large pad pitch. Both the problems lead to difficulties when trying to assemble large detection systems, as needed in order to cover the field of view needed in mammography [174].

In the last chapter, the advantages of three dimensional breast imaging have been discussed. The techniques that allow 3D reconstruction are tomosynthesis and computed tomography. Volumetric imaging has the potential to revolutionize the practice of mammography by providing superior breast cancer detection with no additional radiation exposure and with improved patient comfort compared to conventional mammography [12]. The techniques are expected to enhance the detection of small occult lesions that may be missed by current mammography systems, and to give radiologists an increased confidence in their diagnoses. With respect to tomosynthesis, computed tomography allows quantitative evaluation of the absorption differences between the tissues, which could result in an improvement in the diagnosis.

In this contest, SR breast tomography results particularly promising [13]. The dose is limited thanks to the possibility of selecting the most appropriate energy for the examination. The monochromaticity of the radiation allows also to calculate the absolute values of the attenuation coefficients of tissues, which could be useful for a better discrimination between benign and malignant lesion. Moreover, the spatial resolution of the reconstructed image is enhanced because of the negligible divergence of the beam and scattered radiation is not detected thanks to the beam
laminarity.

The MATISSE detection systems is based on a commercially available fast and low noise counting electronics with full custom read out implemented by means of programmable logic devices. The detector is optimized for tomography, for which the edge on configuration and counting read out present clear advantages [14]. The system is still in the testing and optimization phase. Further improvements are also required in the data acquisition system. The goal is the development of a two layers 20 cm detection system before the end of 2005.

An engineering phase should then start in order to build a detector in order to perform clinical tomographic examinations at the SYRMEP beamline. The examination will consist first in a low dose planar digital scan. A few mammographic slices will be acquired in the regions where the suspicious structures are present. Thanks to its enhanced contrast and to the possibility of tissue characterization, the tomographic examination should help to solve the diagnosis when the nature of the detected lesion is still not clear. The volumetric reconstruction will give to the physicians useful informations on the position and size of the lesions in case a biopsy or surgery has to be performed. The goal is to reduce psychological pain and unnecessary biopsies and treatment in patients with a false-positive diagnosis.
<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
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<tbody>
<tr>
<td>1D</td>
<td>One Dimensional</td>
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<td>2D</td>
<td>Two Dimensional</td>
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<td>3D</td>
<td>Three Dimensional</td>
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<td>AC</td>
<td>Alternate Coupling</td>
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<tr>
<td>ADC</td>
<td>Analog to Digital Converter</td>
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<td>aSe</td>
<td>Amorphous Selenium</td>
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<td>aSi</td>
<td>Amorphous Silicon</td>
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<tr>
<td>ASIC</td>
<td>Application Specific Integrated Circuit</td>
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<td>CMOS</td>
<td>Complementary Metal-Oxide Semiconductor</td>
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<td>CCD</td>
<td>Charged Coupled Device</td>
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<td>C/D</td>
<td>Contrast/Detail</td>
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<td>CT</td>
<td>Computed Tomography</td>
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<td>DAC</td>
<td>Digital to Analog Converter</td>
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<td>DAQ</td>
<td>Data AcQuisition</td>
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<td>DC</td>
<td>Direct Coupling</td>
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<td>DEI</td>
<td>Diffraction Enhanced Imaging</td>
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<td>DEL</td>
<td>Detector ELement</td>
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<td>DM</td>
<td>Digital Mammography</td>
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<td>DMILL</td>
<td>Durci Mixte Isolant Logico Lineaire</td>
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<tr>
<td>DQE</td>
<td>Detected Quantum Efficiency</td>
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<td>DR</td>
<td>Dynamic Range</td>
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<td>DTS</td>
<td>Digital TomoSynthesis</td>
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<tr>
<td>e-h</td>
<td>electron-hole pair</td>
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<td>ENC</td>
<td>Equivalent Noise Charge</td>
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<td>EPROM</td>
<td>Erasable Programmable Read Only Memory</td>
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<td>FF</td>
<td>Fill Factor</td>
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<td>FPGA</td>
<td>Field Programmable Gate Array</td>
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<td>FBGA</td>
<td>Fine Ball Grid Array</td>
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<td>FEL</td>
<td>Free-Electron Laser</td>
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<td>FOM</td>
<td>Figure Of Merit</td>
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<td>FRONTRAD</td>
<td>FRONTier RADiography</td>
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<td>FROST</td>
<td>Frontrad Read Out sySTem</td>
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<td>FWHM</td>
<td>Full Width at Half Maximum</td>
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<tr>
<td>GPIB</td>
<td>General Purpose Interface Bus</td>
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<tr>
<td>GUI</td>
<td>Graphical User Interface</td>
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<tr>
<td>IC</td>
<td>Integrated Circuit</td>
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<tr>
<td>INFN</td>
<td>Istituto Nazionale di Fisica Nucleare</td>
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<tr>
<td>I/O</td>
<td>Input/Output</td>
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<tr>
<td>JFET</td>
<td>Junction Field Effect Transistor</td>
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<td>KES</td>
<td>K-Edge Subtraction</td>
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<td>LAM</td>
<td>Look At Me</td>
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<tr>
<td>Abbreviation</td>
<td>Definition</td>
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<tr>
<td>LVTTL</td>
<td>Low Voltage Transistor-Transistor Logic</td>
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<tr>
<td>LSB</td>
<td>Least Significant Bit</td>
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<tr>
<td>MATISSE</td>
<td>MAmmographic and Tomographic Imaging with Silicon detectors and Synchrotron radiation at Elettra</td>
</tr>
<tr>
<td>MOS</td>
<td>Metal-Oxide Semiconductor</td>
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<tr>
<td>MTF</td>
<td>Modulation Transfer Function</td>
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<tr>
<td>OP-AMP</td>
<td>Operational Amplifier</td>
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<tr>
<td>PC</td>
<td>Personal Computer</td>
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<tr>
<td>PCB</td>
<td>Printed Circuit Board</td>
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<td>PET</td>
<td>Positron Emission Tomography</td>
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<td>PH</td>
<td>Pulse Height</td>
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<td>PhC</td>
<td>Phase Contrast</td>
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<tr>
<td>PLD</td>
<td>Programmable Logic Device</td>
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<tr>
<td>PSF</td>
<td>Point Spread Function</td>
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<tr>
<td>RMS</td>
<td>Root Mean Squared</td>
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<td>RPC</td>
<td>Resistive Plate Chamber</td>
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<td>SF</td>
<td>Screen-Film</td>
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<tr>
<td>SNR</td>
<td>Signal to Noise Ratio</td>
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<td>SPECT</td>
<td>Single Photon Emission Computed Tomography</td>
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<td>SPC</td>
<td>Single Photon Counting</td>
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<tr>
<td>SR</td>
<td>Synchrotron Radiation</td>
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<tr>
<td>SYRMEP</td>
<td>SYnchrotron Radiation for MEdical Physics</td>
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<tr>
<td>TDC</td>
<td>Time to Digital Converter</td>
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<tr>
<td>TDI</td>
<td>Time Delay Integration</td>
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<tr>
<td>TFT</td>
<td>Thin Film Transistor</td>
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<tr>
<td>VHDL</td>
<td>Very high speed integrated circuit Hardware Description Language</td>
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<tr>
<td>VLSI</td>
<td>Very Large Scale of Integration</td>
</tr>
<tr>
<td>VME</td>
<td>VERSA Module Eurocard</td>
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[57] B. Hemdal et al. Mammography - Recent technical developments and their clinical


141, 1999.


