PROCEEDINGS OF SCIENCE

Table-top phase-contrast X-ray microradiography of biological samples with Medipix type detector and flat-panel

Karla Palma-Alejandro[ab*†], **Jan Zemlicka**[a], **Frantisek Krejci**[a] **and Carlos Granja**[a]

[a] *Institute of Experimental and Applied Physics, Czech Technical University in Prague*
Horska 3a/22, CZ-128 00 Prague 2, Czech Republic

[b] *Faculty of Nuclear Sciences and Physical Engineering, Czech Technical University in Prague*
Brehova 7, CZ-115 19 Prague 1, Czech Republic

E-mail: karla.palma@utef.cvut.cz, jan.zemlicka@utef.cvut.cz, frantisek.krejci@utef.cvut.cz, carlos.granja@utef.cvut.cz

Phase-contrast enhanced radiographs of biological samples were obtained using a microfocus X-ray tube, a Timepix/Medipix2, and a flat panel detector. Phase-contrast enhanced images were acquired and evaluated. The image quality was analyzed in terms of signal-to-noise ratio, contrast, spatial resolution, and edge-enhancement for both imagers. Edge-enhancement was obtained from the image intensity profile using oversampling techniques. Superior quality radiographs were obtained with the Medipix type detector.

X Latin American Symposium on Nuclear Physics and Applications (X LASNPA),
1-6 December 2013
Montevideo, Uruguay

*Speaker.

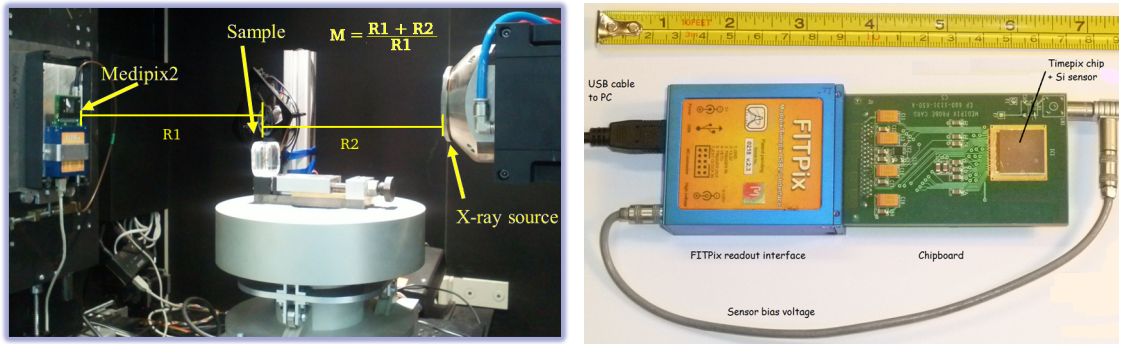
†Supported by CONCIYTEY-CONACYT-Mexico PhD scholarship. Research carried out in frame of the Medipix collaboration.

PoS(X LASNPA)030

1. INTRODUCTION

High resolution radiography is a powerful imaging technique for nondestructive visualization of the fine internal structure of materials and biomedical samples. X-ray imaging is principally based on attenuation, but this can render a difficult task for objects such as soft tissue. This occurs specially when conventional detectors are employed such as charge integrating devices (e.g. CCD's, flat-panel detectors). Improved contrast and high quality radiographs can be obteined by exploting X-ray diffraction techniques (phase-contrast) [1] which require either a coherent X-ray source (synchrotron accelerator) or a highly sensitive detector.
The aim of this work is review the performance [2] of the state-of-the-art X-ray detectors in terms of image quality such as signal-to-noise ratio, contrast, spatial resolution, and newly phase-contrast edge-enhancement. We used two types of digital devices. A flat-panel detector which provides a large sensitive area and a high enough spatial resolution to resolve small objects. However, this charge integrating device suffers from dark current noise and limited dynamic range which limit image quality in terms of contrast, sensititvity, and signal-to-noise ratio (SNR). A solution to these limitations is provided by single-photon counting semiconductor detectors which provide high dynamic range, noiseless (dark current free), and high spatial resolution images.

2. TABLE-TOP MICRORADIOGRAPHY WITH MEDIPIX TYPE DETECTOR AND FLAT-PANEL



(a) (b)

Figure 1: (a) Experimental setup for table-top X-ray microradiography consisting of a microfocus X-ray tube, the sample, and the imager. Magnification (M) is achieved by suitable settings of the relative distances R1 and R2. (b) Radiation camera assembled from the Timepix chip, detector chipboard and FITPix readout interface. Straightforward connection to PC via USB cable.

We used a single-photon counting semiconductor Timepix [3] device equipped with a 300 μm thick silicon sensor. Timepix type detector can be operated as a simple event counter (Medipix2 mode) or as a fully spectroscopic device (TOT mode – time over threshold). The ASIC readout chip is arranged into a matrix of 256×256 pixels (55 μm pitch size and full sensitive area of $1.4 \times 1.4\, cm^2$) fitted with integrated signal electronics per pixel. FITPix interface [4] was used

to communicate with the PC and is controlled by the Pixelman software [5]. We used a Hamamatsu C7942CA flat-panel imager equipped with a scintillator-GOS and with a CMOS sensor (2240×2344 square pixels, $50\,\mu m$ pitch, full sensitive area $11.2 \times 11.7\,cm^2$) used in bin-mode ($100\,\mu m$ pitch). The flat-panel is equipped with an additional thin plastic foil which protects the device. A Hamamatsu L8601-01 microfocus tube was used as the X-ray source, with tungsten (W) transmission anode and a nominal focal spot ($\approx 5\,\mu m$) and divergent cone beam. A geometrically in-line setup [6, 7] was used for magnification projection by changing the distances between source, sample and detector (see Figure 1) regarding each stage of the evaluation ($M = 1$ for SNR & CNR, from $M = 1$ to $M = 30$ for spatial resolution, and $M = 4$ for edge-enhancement). The source-to-detector distance of $67\,cm$ was constant for every stage. Radiograms were acquired with different acquisition times according to each evaluation: for SNR & CNR was used $1\,s$, for spatial resolution and edge enhancement was $150\,s$. Medipix2 was operated at $100\,V$ bias.
After the acquisition, the radiographs were processed by flat-field correction [8], which is the method for suppressing image distortion due to pixel efficiency nonuniformity [9]. For the flat-panel detector the dark current noise is partially supressed by using the algorithm by A. Kwan *et al.* [10]. For the evaluation of the image quality of the detectors we use: the signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR), spatial resolution [11, 2], and edge-enhancement [12].

Signal-to-noise ratio. *It represents a comparison between the level of a desired signal and the level of background noise [11]. We use the equation used by [2].*

$$SNR = \frac{|I_A - I_B|}{\sqrt{{\sigma_A}^2 + {\sigma_B}^2}}, \tag{2.1}$$

Contrast-to-noise ratio. *It is another quantitative measure which describes mainly the density difference between two adjacent areas in the image [11] and is used in [2] as CNR.*

$$CNR = \frac{|I_A - I_B|}{I_A}, \tag{2.2}$$

Spatial Resolution. *It is defined as the full-width half-maximum (FWHM) of a line spread function (LSF) [2]. The LSF can be obtained from the derivative oversampling intensity profile of the radiograph of an edge made of a metalic foil and then fitted by a gaussian function. The FWHM was determined from the sigma parameter of the gaussian function. In this work the influence of the distance between the edge and the tube was evaluated.*

Edge-enhancement. *This is calculated from the oversampling intensity profiles [12] of the object image choosing a region of interest (ROI). Edge-enhancement (EE) can be calculated by:*

$$EE = 100\frac{I_{max} - I_0}{I_0}, \tag{2.3}$$

where I_{max} is the pixel value corresponding to maximum intensity at the edge and I_0 is the background.

Radiological parameters were the same for both detectors. The X-ray tube operating voltage was $40\,kV$. X-ray tube Operating current was $200\,\mu A$ for the SNR & CNR test and edge-enhancement evaluation, and $50\,\mu A$ for the spatial resolution evaluation. The samples used were

$100\,\mu m$ and $200\,\mu m$ thick PMMA foils[1], a $500\,\mu m$ thick steel foil, a plastic fiber of $250\,\mu m$ diameter, and a hair fiber of $60\,\mu m$ diameter.

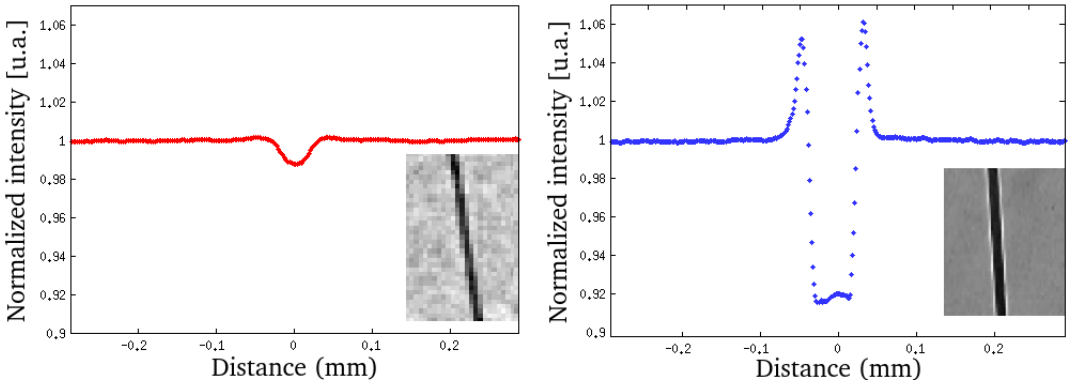
3. RESULTS

SNR and CNR values were obtained from ROIs outlined on $100\,\mu m$ (A) and $200\,\mu m$ (B) PMMA foils, using A as reference the background.

Table 1: Comparative results of X-ray microradiographs acquired by Medipix2 and flat-panel detectors.

Detector	**SNR**	**CNR**	**Spatial Resolution**		**Edge Enhancement**	
			$M=1$	$M\approx 30$	**Plastic**	**Hair**
Medipix2	2.8	$(4.11\pm0.04)\%$	$31.8\pm4.6\,\mu m$	$4.6\pm0.6\,\mu m$	10.5%	5.7%
Flat-panel	0.4	$(0.5\pm0.1)\%$	$126.8\pm7.6\,\mu m$	$5.4\pm0.9\,\mu m$	0.4%	0.1%

The evaluation of the system spatial resolution for both detectors, was done by increasing the geometrical magnification, and the maximun resolution was given by Medipix2. Oversampling intensity profiles were computed using *Sool'Oochel-Profile* matlab code [12] in order to estimate the edge-enhancement. Figure 2 shows the oversampling intesity profiles at the same scale from radiographs of hair fiber acquired with Medipix2 and flat-panel detectors. From this picture the minimun peaks can be seen using Medipix2. The edge-enhancement of plastic and hair fibers showed higher values for acquisitions with Medipix2. The plastic fiber is thicker than the hair fiber and the EE results show higher values for the plastic fiber than for the fiber of hair; for both detectors, it agreed with the results showed by [12]. The absortion-contrast measured as the minimal value in the U-shape of the fiber profile was always lower for acquisitions with flat-panel than with Medipix2. Figure 3 shows radiographs of a bee acquired with both Medipix and

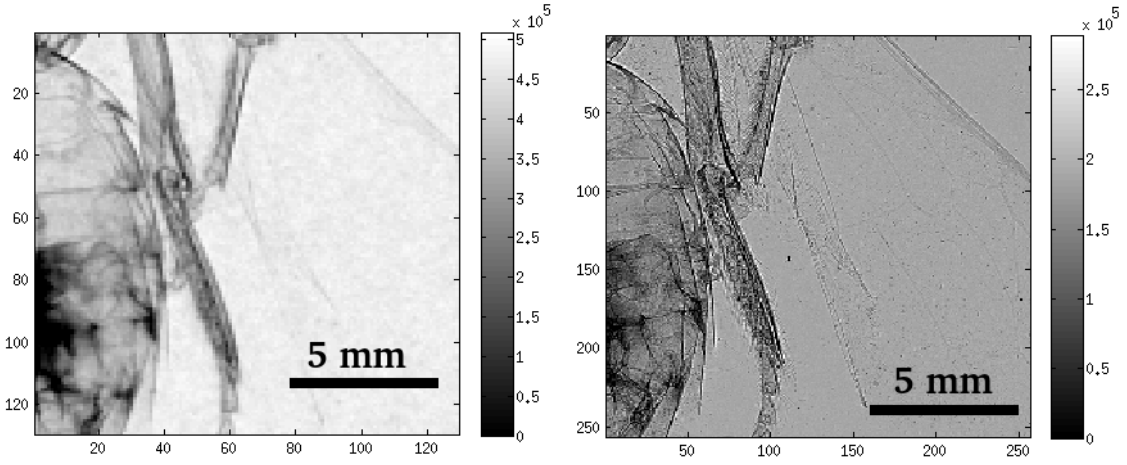


(a) (b)

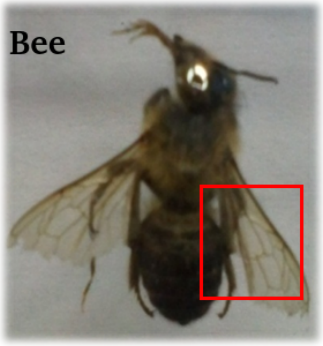
Figure 2: Oversampling intensity profiles of X-ray microradiographs of a hair fiber ($60\mu m$) with the (a) flat-panel and (b) Medipix2 detectors. Acquisition paramenters were $40\,kV$, $30\,mAs$, $M=4$, and $R1+R2=67\,cm$.

[1]PMMA foils were the same used by Ref. [2] which have attenuation properties similar to the soft biological tissue.

flat-panel detectors. Radiographs of a biological sample (bee) demostrate the higher performance of Medipix2, with operating voltage $40\,kV$, operating current $200\,\mu A$, exposition time $125\,s$, and $M = 3$.



(a) (b)



(c)

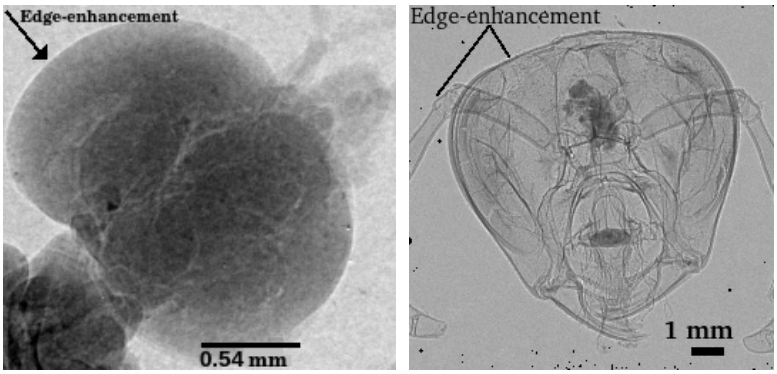
Figure 3: Microradiographs of a part of a bee outlined by a red square (photo included (c)) acquired by the (a) flat-panel and (b) Medipix2 detectors. The contrast and intensity color depth of the Medipix2 image are significatly greater than for the flat-panel.

Figure 4 shows microradiographs of two samples, the heads of a fly and of a wasp. Fly's head was acquired with flat-panel detector and the wasp's head with Medipix2 under the same radiological parameters.

From the Figures 3 and 4 it can be seen that the radiographs obtained with Medipix2 provides higher contrast and reveals more details from the phase effects.

Figure 5 shows a high resolution radiographs acquired with Medipix type detectors (Medipix2 and Timepix-Quad[1] [13]). Fine structures as hair can be seen in Figure 5(b).

[1]Timepix-Quad detector is built of four standard Timepix read-out chips bump-bonded to a single common sensor layer ($300\,\mu m$ silicon) which give an array of 256×1024 pixels ($55\,\mu m$ pixel pitch) in a total sensitive area of $7.84\,cm^2$.



(a) (b)

Figure 4: (a) Microradiograph of the head of a fly acquired by the flat-panel detector. (b) Microradiograph of the head of a wasp captured by Fitpix/Medipix2 imager. For both acquisitions the radiological parameters were $50\,kV$, $150\,\mu A$, $50\,s$ exposition time, $R1+R2=60\,cm$, and $M=3.5$.

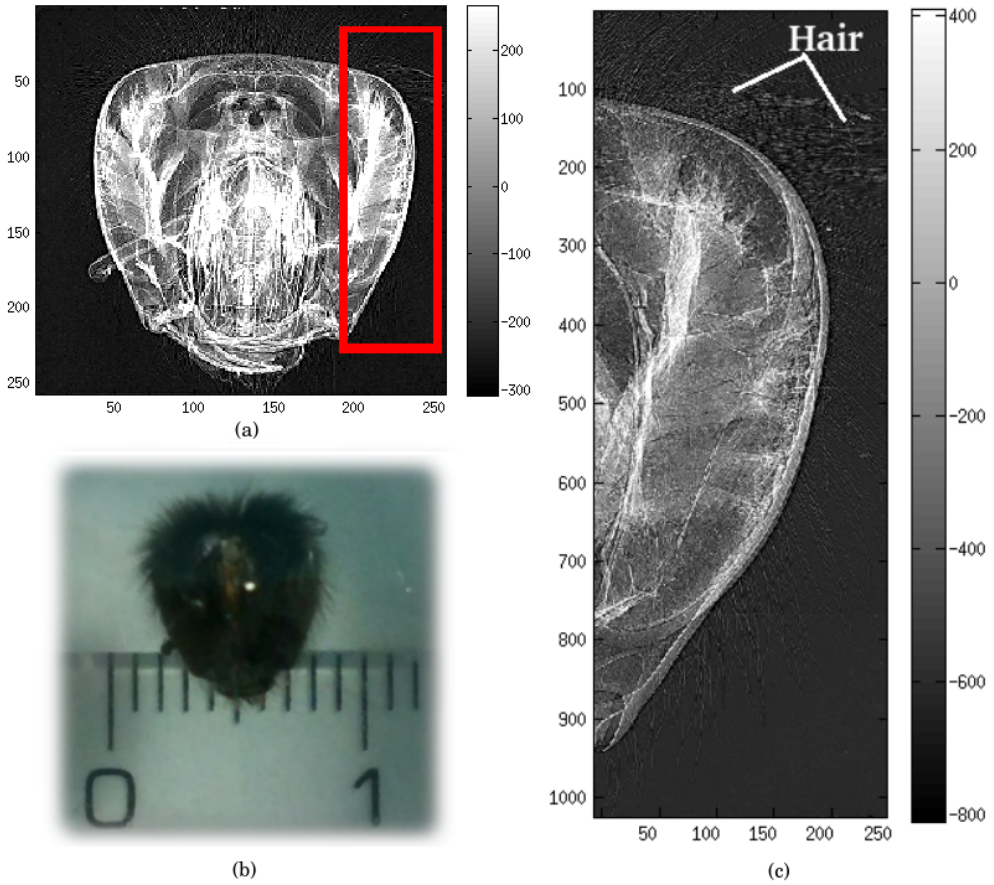


Figure 5: (a) Microradiograph of the head of a queen honey-bee (photo included in (b)) acquired by Medipix2 at $M=2$. (c) Microradiograph of the of a part of the head of the same queen honey-bee (outlined by a red square in (a)) acquired with Timepix-Quad detector [13] at $M=9$. Radiological parameters of the radiographs were $40\,kV$, $200\,\mu A$, $125\,s$, and $R1+R2=67\,cm$.

4. CONCLUSIONS

High quality microradiographs were produced in the low energy range to image biological samples confirming that particle counting detectors are preferable for high spatial resolution and contrast enhanced microradiography. Comparared to the flat-panel imager, Medipix type detector provides a higher performance thanks to the quantum–counting and noiseless integration together with broad (unlimited) dynamic range. For weakly attenuating objects SNR and CNR were ≈ 7 and ≈ 8 times, respectively, higher for Medipix2; edge-enhancement was > 50 times higher for plastic fiber, and > 25 times for hair. Also, results showed that for larger magnifications Medipix type detector is able to resolve smaller objects (higher spatial resolution of the system). Phase-contrast was effectively used as a technique to improve contrast in the acquired images.

References

[1] J. Jakubek, C. Granja, J. Dammer, R. Hanus, T. Holy, S. Pospisil, R. Tykva, J. Uher and Z. Vykydal, *Phase contrast enhanced high resolution X-ray imaging and tomography of soft tissue*, *Nucl. Instr. and Meth. Phys. A*, **571** (2007) 69–72.

[2] P.M. Frallicciardi, J. Jakubek, D. Vavrik and J. Dammer, *Comparison of single-photon counting and charge-integrating detectors for X-ray high-resolution imaging of small biological objects*, *Nucl. Instr. and Meth. Phys. A*, **607** (2009) 221–222.

[3] X. Llopart, M. Campbell, R. Dinapoli, D. San Segundo and E. Pernigotti, *Medipix2: A 64-k pixel readout chip with* $55-\mu m$ *square elements working in single photon counting mode*, *IEEE Trans. Nucl. Sci.*, **49** (2002) 2279–2283.

[4] V. Kraus, M. Holik, J. Jakubek, M. Kroupa, P. Soukup and Z. Vykydal, *FITPix– fast interface for Timepix pixel detectors*, *JINST*, **6** (2011) C01079.

[5] D. Turecek, T. Holy, J. Jakubek, S. Pospisil and Z. Vykydal, *Pixelman: a multi-platform data acquisition and processing software package for Medipix2, Timepix and Medipix3 detectors*, *JINST*, **6** (2011) C01046.

[6] R. Fitzgerald, *Phase-Sensitive X-Ray Imaging*, *Physics Today*, **53** (2000) 23–26.

[7] S.W. Wilkins, T.E. Gureyev, D. Gao, A. Pogany and A.W. Stevenson, *Phase-contrast imaging using polychromatic hard X-rays*, *Naturec*, **384** (1996) 335–338.

[8] J.A. Seibert, J.M. Boone and K.K. Lindfors, *Flat-field correction technique for digital detectors*, in proceedings of *Physics of Medical Imaging-SPIE*, **3336** (1998) 348–354.

[9] L. Tlustos and E.H.M. Heijne, PhD thesis *Performance and limitations of high granularity single photon processing X-ray imaging detectors*, Vienna, Tech. U. 2005.

[10] A.L.C. Kwan, J.A. Seibert and J.M. Boone, *An improved method for flat-field correction of flat panel X-ray detector*,*Med. Phys.*, **33** (2006) 391–393.

[11] J.T. Bushberg, J.A. Seibert, E.M. Leidholdt and J.M. Boone, *The Essential Physics of Medical Imaging*, 2nd edition, Lippincott Williams and Wilkins, USA 2001 .

[12] K.D. Palma-Alejandro, T. Murrieta and M.E. Brandan, *Use of oversampling to quantify phase effects in X-ray images of straight fibers*, *Nucl. Instr. and Meth. Phys. A*, **701** (2013) 201–207.

[13] Medipix collaboration website at http://medipix.web.cern.ch/MEDIPIX/