A Large Area GEMPix detector for treatment plan verification in hadron therapy

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Abstract. Quality Assurance in hadron therapy is crucial to ensure a safe and accurate dose delivery to the patients. This requires fast and reliable detectors with high spatial resolution. A first LaGEMPix prototype that combines a triple Gas Electron Multiplier and a highly pixelated readout based on a matrix of organic photodiodes coated on an oxide thin film transistor backplane has been built. The first version of the LaGEMPix has proven to have a limited spatial resolution, mainly attributed to the isotropic emission of the scintillation photons within the GEM holes. To improve the spatial resolution and confirm our predictions of the role of the photons, we built a new version of the detector with a reduced gap between the last GEM foil and the readout. Experimental results acquired using different methods and experimental set-ups show that the spatial resolution significantly improved with the new design.

1. Introduction

Hadron therapy is an advanced radiotherapy technique that offers significant benefits over traditional photon and electron treatments, and is rapidly gaining popularity as one of the radiation modalities for cancer treatment [1]. The physical properties of hadrons, predominantly protons and carbon ions, produce better dose distributions and improve treatment of some tumors [2], with better sparing of the healthy tissue.

Treatment with hadrons requires not just high spatial resolution, but also exceptionally accurate dose calculation in order to accomplish optimal dose delivery. A high spatial resolution of the 2D dose distribution is essential since most of the treatment plans in Pencil Beam Scanning (PBS) are delivered through a large number of small beams with varying intensity to treat small well-defined lesions [3]. The treatment can involve very high "in-field" dose gradients, up to 15%/mm in intensity modulated proton therapy (IMRT), with the purpose of accomplishing high conformity to the planning target volume (PTV) [4, 5]. It is therefore crucial that the required dose is delivered exactly where prescribed (in the PTV) to spare the healthy tissue and/or organs at risk. This is ensured by appropriate quality assurance (QA) techniques and tools. To accomplish an efficient QA procedure, detectors for measuring the relevant beam characteristics, in particular beam position and delivered dose, is needed [6]. Nowadays, improvements are still possible towards an all-in-one solution providing accurate and real-time measurements with submillimeter spatial resolution, and a uniform response to the beam energy. QA programs based on different types of detectors can be very complex and time consuming. A single solution that includes all the information will minimize the equipment costs, the setup time and therefore the necessary resources in the treatment facility, improving the overall performance of the QA programs [7, 8, 9].

1.1. LaGEMPix: original version

A promising tool for more efficient QA procedures with high spatial resolution is the LaGEMPix detector (figure 1). It consists of a triple-GEM (Gas Electron Multiplier) [10] coupled to a highly pixelated readout based on a matrix of organic photodiodes (OPDs). Scintillation photons generated in the GEM holes after electron avalanche multiplication are detected by the matrix of OPDs, placed at 3 mm from the production point. A more detailed description of the LaGEMPix and the results summarized in the following can be found in reference [11].

The detector was characterized using low energy X-rays (30-40 kV) at the Calibration Laboratory of CERN Radiation Protection Group [12]. Extensive measurements to determine the spatial resolution for various experimental configurations were performed. The detector's spatial resolution was evaluated using three different methods: (1) calculating the Edge Spread Function (ESF) along the sharp edge of a 2.5 cm thick lead block, (2) measuring the Line Spread Function (LSF) and distance between adjacent holes using two copper masks with holes of different sizes and spacing, and (3) determining the Modulation Transfer Function (MTF) of a commercial lead plate. Results showed that the ESF underestimated the spatial resolution, yielding a resolution of 9.70 ± 0.09 mm for 40 kV X-rays. The LSF method revealed that the LaGEMPix was able to resolve two 5 mm holes separated by 3 mm. However, a limitation was observed with the MTF, which showed that slits separated by 2 mm were not distinguishable. From these measurements we concluded that the spatial resolution achieved with the first version of the LaGEMPix was not as high as needed for QA in hadron therapy and therefore, some modifications were planned based on the following considerations.

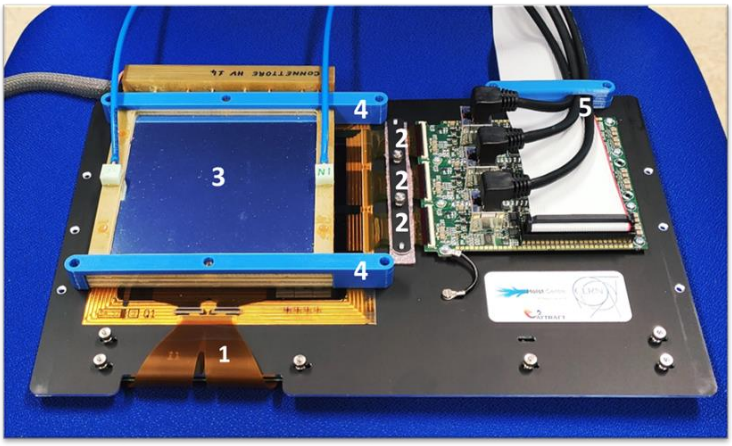


Figure 1. The LaGEMPix prototype [11]: (1) flex gate driver integrated circuit; (2) flex Read-out Integrated Circuits (ROICs); (3) the triple-GEM 10 x 10 cm^2 stack coupled to the optical readout with the thin Mylar window on top; (4) 3D-printed braces to hold together the triple-GEM detector and the image sensor; (5) cables to connect the detector to the readout system.

A comparison with GAFCHROMIC® films [13], the GEMPix detector [14] – a triple-GEM stack coupled to a pixelated charge readout –, and Monte Carlo simulations using FLUKA [15] showed that the main contribution to the spatial resolution is most likely the isotropic emission of the scintillation photons. It should be emphasized that even if, to date, there is no precise information in the literature regarding the directionality of light emission in GEM-based detectors, there is a consensus that photons are emitted isotropically [16, 17, 18]. Based on this assumption and on the obtained results, we concluded that the isotropic emission of the scintillation light introduces an additional blurring in the image, worsening the spatial resolution measured with the lead block from 5.20 ± 0.10 mm (GEMPix) to 9.70 ± 0.09 mm (LaGEMPix). The isotropic emission of photons is unavoidable. Its impact on the spatial resolution is determined by the distance between the points where photons are produced and detected. To prove our hypothesis and to reduce its effect, we modified the design of the LaGEMPix by decreasing the distance between the last GEM (GEM3) and the readout plane. This modification will reduce the dispersion of the light before reaching the readout.

2. Materials and methods

2.1. Detector design

A new detector prototype featuring a reduced distance between GEM3 and the readout was built. Figure 2 shows the schematic details of the new design. The reduction of the distance from 3 to 1.5 mm was achieved by (1) changing the gap between the GEM3 and the anode, known as induction gap, from 2 mm to 1 mm and (2) by replacing the indium tin oxide (ITO) transparent electrode, coated on a 1.1 mm thick fused quartz substrate, with an ITO electrode coated on a 0.5 mm thick fused silica substrate. The new transparent electrode is also more radiation resistant according to recent measurements [19]. Due to mechanical reasons it was not possible to further reduce these distances. A glass substrate thinner than 0.5 mm would be extremely fragile causing problems during the production, coating and assembly procedures. In addition, the last GEM surface might exhibit a slight bend which had to be taken into consideration in order to avoid contact with the ITO anode.

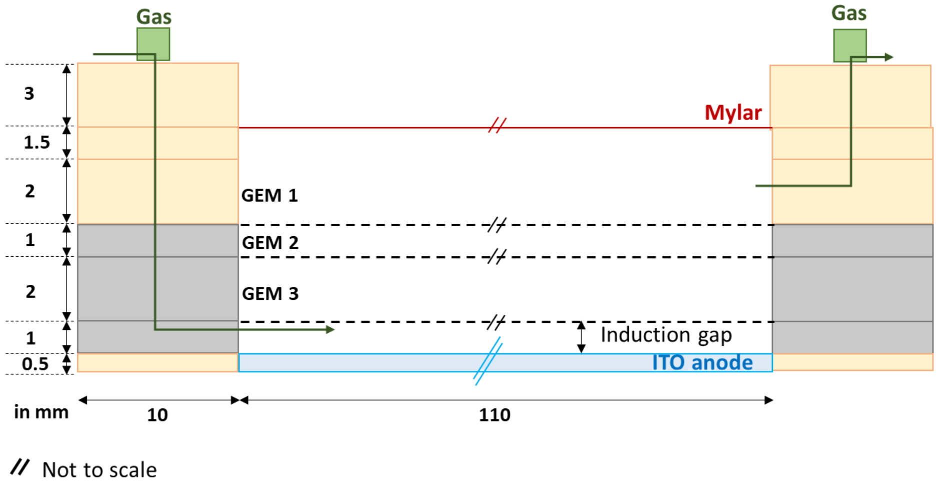


Figure 2. Schematic diagram of the improved design of the LaGEMPix detector.

2.2. Experimental set-up

The spatial resolution of the LaGEMPix has been evaluated with 30 kV and 40 kV X-rays from an X-ray generator, Model X80-320kV from Hopewell Designs, Inc. This system, equipped with 10 Narrow Spectra Filters (N-series), was used to provide X-rays in compliance to the ISO 4037 standard [20]. More specifically, the Hopewell N-5 and N-6 filters, matching to the N-30 and N-40 ISO 4037 standard, respectively, were chosen.

Measurements similar to those reported in [11] were carried out with the new detector. For the ESF, we placed a lead block of 10 x 20 x 2.5 cm^3 dimensions in front of the detector, covering part of its active area. A region of interest (ROI) was set perpendicularly to the edge, and the edge response profile was calculated from the average of 200 background corrected images. The spatial resolution was estimated by fitting the edge profile by a logistic function [11, 21].

The LSF was measured using a 3 mm thick copper plate placed at 7 mm from the Mylar window. The mask has several holes of 5 mm diameter spaced by 3 to 7 mm, edge to edge. This method allowed to evaluate the capability of the LaGEMPix to resolve adjacent holes. Finally, we placed various X-ray test patterns in front of the Mylar window to calculate the MTF.

3. Results

The experimental conditions were identical as in [11]: 30 kV (N-5 series filter) or 40 kV X-rays (N-6 series filter), minimum aperture of 1 cm, 230 cm source-detector distance and same electric fields in the GEM structure: transfer field 1 = 2.0 kV/cm; transfer field 2 = 1.75 kV/cm; induction field = 5.0 kV/cm; drift field = 1 kV/cm. The electric fields between the top and bottom copper layers in each GEM foil were kept constant corresponding to a total voltage of 940 V.

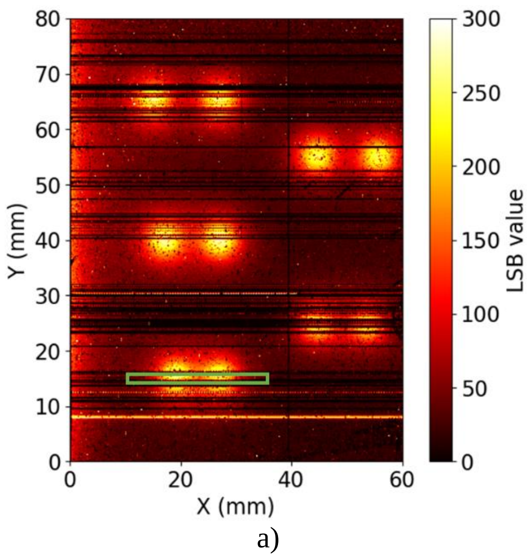
3.1. Edge spread function (ESF)

The new detector shows a slight improvement on the spatial resolution when using the ESF. Results show an FWHM of 8.17 ± 0.07 mm compared to 9.70 ± 0.09 mm obtained with the first version of the detector.

3.2. Line spread function (LSF)

The upgraded detector presents an enhanced spatial resolution when using the LSF. Since the average image profile on a single hole is Gaussian, the spatial resolution was assessed by fitting the LSF by a Gaussian function and determining the FWHM of a 5 mm diameter hole. The obtained FWHM using the new version of the LaGEMPix was 5.61 ± 0.14 mm compared to 6.73 ± 0.08 mm previously measured.

Additionally, a ROI was selected at the centre of the 5 mm holes spaced by 3 mm (edge to edge) as depicted by the green region in figure 3a). Figure 3b) compares the line-average response profile of two holes spaced by 3 mm for the original and upgraded versions, featuring two peaks with a dip in the intensity. Two holes of 5 mm diameter at a distance of 3 mm can be resolved by both detectors, however figure 3b) shows a more pronounced dip in the intensity with the upgraded version of the LaGEMPix and consequently an improvement of the LSF.



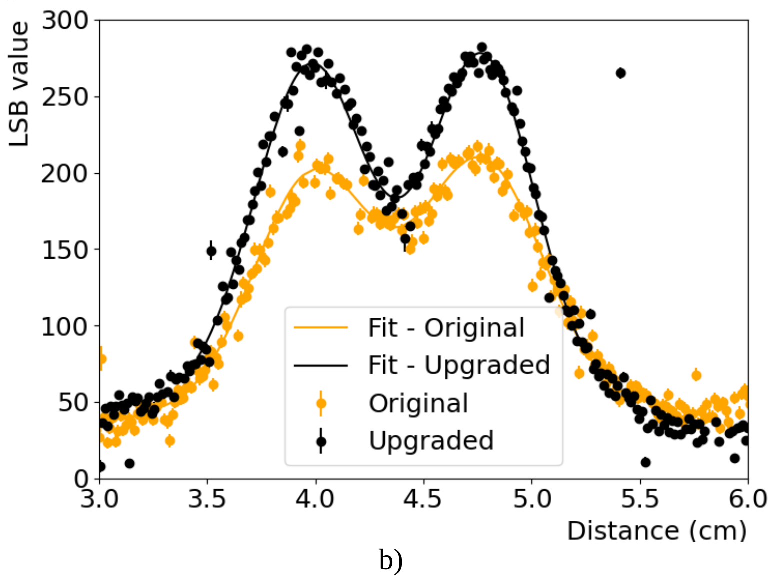


Figure 3. a) Heat map of the copper mask for 40 kV X-rays. A ROI (green rectangle) was set on the holes separated by 3 mm. The spatial resolution was estimated by fitting the profile in the ROI by a Gaussian function. b) The line-average response profile of 5 mm diameter holes spaced by 3 mm (edge to edge) for the original (orange) and upgraded (black) versions of the LaGEMPix. The FWHM obtained by the Gaussian distribution for the upgraded version is 6.16 ± 0.13 mm for the left hole and 5.75 ± 0.15 mm for the right hole. The distance (centre-to-centre fit) of 7.86 mm was obtained by fitting the profile by a double Gaussian function.

3.3. Modulation Transfer Function (MTF)
These tests were carried out using 30 kV X-rays with the N-5 filter in order to increase the contrast of the output image. The mask is made of lead with 0.2 mm thickness and resolution ranging from 0.177 to 3.33 LP/mm, as shown in figure 4, with the larger line spacing being 2.8 mm [22].

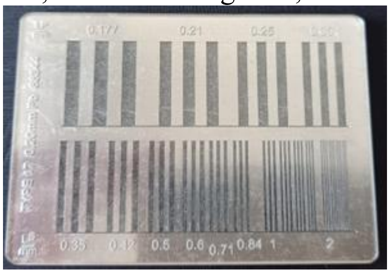


Figure 4. Line pair mask type 17 made of 0.02 mm thick lead used as an imaging target. For this particular mask, 0.5 LP/mm means that one black and one white line within 2 mm will be projected on the image sensor.

As can be clearly seen in figure 5, an improvement was obtained with the new detector. The upgraded version of the LaGEMPix is able to distinguish 0.21 LP/mm, which corresponds to two slits separated by 2.4 mm. A limit is observed at 0.25 LP/mm (two slits separated by 2 mm). The first version of the LaGEMPix was, on the other hand, unable to resolve 0.177 LP/mm, corresponding to two slits separated by 2.8 mm.

Table 1 summarizes the values of spatial resolution obtained for the various detectors and experimental configurations. As expected, the upgraded LaGEMPix with reduced gap exhibits the best spatial resolution. A more detailed discussion of the different methods presented here can be found in [11].

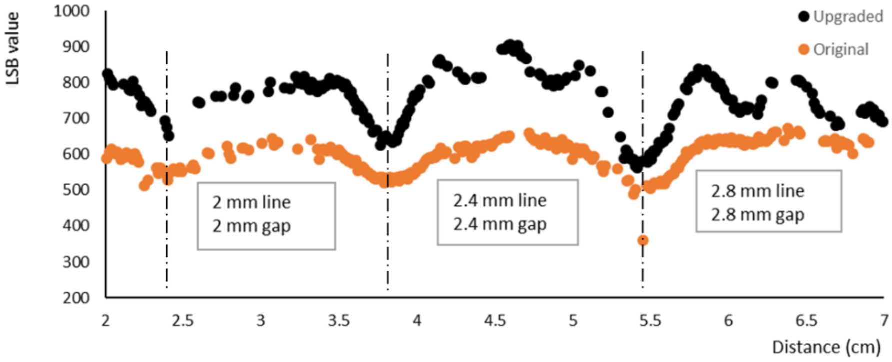


Figure 5. The line-average response profile of line pair mask type 17 with original version of LaGEMPix (orange) versus upgraded LaGEMPix (black).

Table 1. Summary of the spatial resolution obtained for different experimental configurations and by both versions of the LaGEMPix.

	Spatial Resolution (mm)			
Detector	**Edge Response**	**5 mm Cu hole**	**Minimum resolvable hole spacing**	**MTF mask limit**
Original LaGEMPix [11]	9.70 ± 0.09	6.73 ± 0.08	3 mm (edge to edge)	<0.177 LP/mm
Upgraded LaGEMPix	8.17 ± 0.07	5.61 ± 0.14	3 mm (edge to edge)	0.21 LP/mm

4. Conclusion
An upgraded version of the LaGEMPix has been developed, featuring a reduction of the distance between the light production and optical readout by a factor of two compared to the first version of the detector. Similar to the original prototype, the new detector has been characterized using low energy X-rays and different methods to determine the spatial resolution. The results shown in this paper demonstrate that the distance between the last GEM and the imager has an impact on the measured spatial resolution. A decrease in GEM-readout distance resulted in a spatial resolution of 0.21 LP/mm, corresponding to two slits separated by 2.4 mm in a line pair mask. Since the distance between the last GEM and the readout cannot be further reduced due to mechanical reasons, a submillimetre spatial resolution is hardly reachable for an optical readout without the introduction of lenses.

Commercial vendors, such as PTW[1] and IBA[2], define the spatial resolution of their clinical detectors used in hadron therapy by the pixel size or pixel pitch. For example, IBA states that the spatial resolution of myQA® Phoenix for proton therapy is 0.2 mm [23]. The pixel pitch of the LaGEMPix is 126 µm. However, this results in a spatial resolution of 2.4 mm using X-Rays, as stated above. Studies using protons in order to directly compare with the detectors in clinical use are foreseen.

As the isotropic emission of the scintillation light was identified as the main limitation to the achievable spatial resolution, a charge readout is currently being considered. In this case, secondary electrons produced in the GEMs and guided by electric fields to preserve the spatial resolution would be directly detected by the readout. Based on the GEMPix results and the FLUKA Monte Carlo simulation [11], the targeted sub-millimetre resolution is expected.

References

[1] Particle Therapy Co-Operative Group - Particle therapy facilities in clinical operation (last update: June 2021) . Available online: https://www.ptcog.ch/index.php/facilities-in-operation (accessed June. 5, 2021)

[2] Ishikawa H, Nakai K, Nonaka T and Sakurai H 2019 Particle Therapy in Cancer Treatment-Current and Future Perspective *Gan To Kagaku Ryoho* **46** 1219–25

[3] Journal of the ICRU Report 78 *Oxford University Press* **7** 2

[4] Molinelli S, Mairani A, Mirandola A, Vilches Freixas G, Tessonnier T, Giordanengo S, Parodi K, Ciocca M and Orecchia R 2013 Dosimetric accuracy assessment of a treatment plan verification system for scanned proton beam radiotherapy: one-year experimental results and Monte Carlo analysis of the involved uncertainties *Phys Med Biol* **58** 3837–47

[5] Winter J, Ellerbrock M, Jäkel O, Greilich S and Bangert M 2020 Analytical modeling of depth-dose degradation in heterogeneous lung tissue for intensity-modulated proton therapy planning *Physics and Imaging in Radiation Oncology* **14** 32–8

[6] Mirandola A, Molinelli S, Vilches Freixas G, Mairani A, Gallio E, Panizza D, Russo S, Ciocca M, Donetti M, Magro G, Giordanengo S and Orecchia R 2015 Dosimetric commissioning and quality assurance of scanned ion beams at the Italian National Center for Oncological Hadrontherapy *Med Phys* **42** 5287–300

[7] Zhu X Ronald, Li Y, Mackin D, Li H, Poenisch F, Lee A K, Mahajan A, Frank S J, Gillin M T, Sahoo N and Zhang X 2015 Towards Effective and Efficient Patient-Specific Quality Assurance for Spot Scanning Proton Therapy *Cancers (Basel)* **7** 631–47

[8] Lambert J, Bäumer C, Koska B and Ding X 2014 Daily QA in proton therapy using a single commercially available detector *Journal of applied clinical medical physics / American College of Medical Physics* **15** 5005

[9] Hernandez Morales D, Shan J, Liu W, Augustine K E, Bues M, Davis M J, Fatyga M, Johnson J E, Mundy D W, Shen J, Younkin J E and Stoker J B 2019 Automation of routine elements for spot-scanning proton patient-specific quality assurance *Med Phys* **46** 5–14

[10] Sauli F 2016 The gas electron multiplier (GEM): Operating principles and applications *Nucl. Instr. Meth. A* **805** 2–24

[11] Maia Oliveira A, B Akkerman H, Braccini S, van Breemen J J M, Gallego Manzano L, Heracleous N, Katsouras I, Leidner J, Murtas F, Peeters B and Silari M 2021 Characterization with X-rays of a Large-area GEMPix detector with optical readout submitted to Special Issue Detectors for Medical Physics of Applied Sciences.

[12] Brugger M, Carbonez P, Pozzi F, Silari M and Vincke H 2014 New radiation protection calibration facility at CERN *Radiat Prot Dosimetry* **161** 181–4

[13] Gafchromic™ XR film State-of-the-art processor-less products for radiology applications

[1] PTW-Freiburg, Lörracher Strasse 7, 79115 Freiburg, Germany, Web: https://www.ptwdosimetry.com/

[2] IBA Dosimetry, Bahnhofstraße 5, 90592 Schwarzenbruck, Germany, Web: https://www.iba-dosimetry.com/

Available online: http://www.gafchromic.com/documents/PC-11805_Gafchromic_XR.pdf (accessed June. 19, 2021)
[14] Leidner J, Ciocca M, Mairani A, Murtas F and Silari M 2020 A GEMPix-based integrated system for measurements of 3D dose distributions in water for carbon ion scanning beam radiotherapy *Medical Physics* **47** 2516–25
[15] Home | The Official CERN FLUKA Website Available online: https://fluka.cern/ (accessed on 21 June 2021).
[16] Oliveira C A B, Correia P M M, Schindler H, Ferreira A L, Monteiro C M B, Santos J M F dos, Biagi S, Veenhof R and Veloso J F C A 2012 Simulation of VUV electroluminescence in micropattern gaseous detectors: the case of GEM and MHSP *J. Inst.* **7** P09006–P09006
[17] Fraga F A F, Fetal S T G, Fraga M M F R, Balau E F S, Margato L M S, Marques R F, Policarpo A J P L and Sauli F 2004 The scintillation of GEMS coated with wavelength shifters *Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment* **525** 57–61
[18] Klyachko A V, Moskvin V, Nichiporov D F and Solberg K A 2012 A GEM-based dose imaging detector with optical readout for proton radiotherapy *Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment* **694** 271–9
[19] Maia Oliveira A, Braccini S, Casolaro P, Heracleous N, Leidner J, Mateu I, Murtas F and Silari M 2021 Radiation-induced effects in glass windows for optical readout GEM-based detectors *arXiv:2106.04645 [physics]* (accepted for publication in JINST).
[20] ISO 4037-2:2019, Radiological protection — X and gamma reference radiation for calibrating dosemeters and doserate meters and for determining their response as a function of photon energy — Part 2: Dosimetry for radiation protection over the en-ergy ranges from 8 keV to 1,3 MeV and 4 MeV to 9 MeV
[21] Energy Resolution Due to Thermal Broadening (STM) Available online: https://shunchi100.wordpress.com/physics-research/energy-resolution-thermal-broadening/ (accessed on 22 June 2021)
[22] Line Pair Patterns - Test Phantoms | QUART X-Ray QA QC Solutions Available online: https://quart.de/en/products/test-phantoms/resolution-patterns/line-pair-patterns (accessed on 21 June 2021)
[23] GmbH, I.D. Product myQA® Phoenix High-resolution digital detector array Available online: https://www.iba-dosimetry.com/product/myqa-phoenix/ (accessed on 22 October 2021)