PAPER

Exploration of different x-ray Talbot–Lau setups for dark-field lung imaging examined in a porcine lung

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Abstract

X-ray dark-field imaging is a promising technique for lung diagnosis. Due to the alveolar structure of lung tissue, a higher contrast is obtained by the dark-field image compared to the attenuation image. Animal studies indicate an enhancement regarding the detection of lung diseases in early stages. In this publication, we focus on the influence of different Talbot–Lau interferometer specifications while maintaining the x-ray source, sample magnification and detector system. By imaging the same porcine lung with three different grating sets, we analyze the contrast-to-noise ratio of the obtained dark-field images with respect to visibility and correlation length. We demonstrate that relatively large grating periods of the phase and of the analyzer grating are sufficient for high quality lung imaging at reasonable dose levels.

1. Introduction

Contrast in clinical x-ray imaging is based on differences of the attenuation coefficient of the imaged materials. The attenuation coefficient is proportional to the imaginary part of the complex refractive index. It depends mainly on the atomic number Z of the corresponding material (Als-Nielsen and McMorro 2011). Hence, a high contrast, e.g. between bone and surrounding soft tissue can be observed. Whereas, the composition of light elements of similar density leads to a poor contrast in conventional x-ray radiography.

On that account, phase-sensitive imaging techniques are advantageous (Fitzgerald 2000). As mentioned, the attenuation of x-rays is described by the imaginary part of the complex refractive index. The real part provides information about refraction of an electromagnetic wave within matter which can be inferred from the phase-contrast image. It enhances differences between light elements and therefore, enables a better soft tissue contrast (Momose 1995). Different methods of phase-sensitive imaging techniques with x-rays have been developed employing various approaches (Bonse and Hart 1965, Snigirev *et al* 1995, Momose *et al* 1996, Chapman *et al* 1997, Olivo *et al* 2001, David *et al* 2002, Weitkamp *et al* 2005).

In 2003 the grating-based Talbot interferometry was employed for x-ray imaging by using synchrotron radiation (Momose *et al* 2003). In order to enable the usage of x-ray phase-contrast imaging for clinical applications, first results were published in Weitkamp *et al* (2005) demonstrating that broad polychromatic x-ray spectra are usable. Conventional laboratory x-ray sources with a large focal spot are applicable due to the condition of Lau (1948) by inserting a source grating into the grating-based setup (Pfeiffer *et al* 2006). By using such a setup, the differential phase image and the dark-field image which was introduced in Pfeiffer *et al* (2008), are obtainable simultaneously to the conventional attenuation image. Thus, extended information about a sample is gained with the help of a laboratory Talbot–Lau interferometer, leading to a variety of application possibilities for non-destructive testing (Kastner *et al* 2012, Nielsen *et al* 2013, Prade *et al* 2017, Ludwig *et al* 2018) and medical imaging.

In particular, x-ray dark-field imaging is sensitive to small porous or fibrous structures even at sub-pixel scales (Revol *et al* 2011). This opens up new possibilities for improved diagnosis in medical imaging. In

Yaroshenko *et al* (2014) an overview about recent results and promising applications in biomedical imaging for x-ray dark-field imaging is given. Investigations in mammography (Stampanoni *et al* 2011, Michel *et al* 2013) demonstrated that dark-field imaging is a promising field of application. Furthermore, the detectability of foreign particles, e.g. a wooden splinter in a pork trotter (Rieger *et al* 2017), is considerably enhanced by means of the strong dark-field signal occurring due to the fibrous wooden structure.

Moreover, lung imaging seems to be one of the most promising applications for x-ray dark-field imaging (Weber *et al* 2012, Einarsdóttir *et al* 2015, Hellbach *et al* 2017). Since imaging of lungs requires a differentiation of different soft tissue types which only slightly differ with respect to the attenuation coefficients, the detection of lung diseases by conventional attenuation radiography is challenging. However, the air-tissue boundaries of the lung alveoli generate a strong dark-field signal. The loss in alveoli structure because of some lung disease enables the detection of destroyed tissue by a significantly decreased dark-field signal earlier than in attenuation imaging as the dark-field signal is more sensitive to slight changes of the alveoli structure.

Investigations of *in vivo* lung imaging (Bech *et al* 2013, Hellbach *et al* 2015) and diagnosis of lung cancer in mice (Gromann *et al* 2017b, Scherer *et al* 2017) have been shown in several publications. In order to investigate the feasibility of clinical applicability, images of an *ex vivo* pig's lung followed (Gromann *et al* 2017b). Recently, also results about Talbot–Lau imaging of an *in vivo* pig's lung (Gromann *et al* 2017a) and the first x-ray dark-field images of *in situ* human lungs in a deceased body (Willer *et al* 2018) were published.

Up to now x-ray dark-field imaging shows advantages for the detection of pulmonary emphysema (Schleede *et al* 2012, Yaroshenko *et al* 2013, Meinel *et al* 2014, Hellbach *et al* 2015), the diagnosis of pneumothorax (Hellbach *et al* 2016, Hauke *et al* 2018, Hellbach *et al* 2018a, Seifert *et al* 2018) and the early detection of pulmonary fibrosis (Hellbach *et al* 2017). Furthermore, the results on the diagnosis of neonatal injuries (Yaroshenko *et al* 2016) and the observation of the stage of lung inflammation (Hellbach *et al* 2018b) have been reported.

With regard to the clinical applicability of pulmonary x-ray dark-field imaging, we investigate the influence of the interferometer specifications regarding the dark-field signatures of lung tissue. Therefore, a porcine lung has been imaged by applying three different grating sets, where the analyzer grating period varies from 2.4 μm to 4.8 μm and 10 μm . We analyze the obtained dark-field images of the porcine lung for each setup by looking at visibility, correlation length, contrast-to-noise ratio and reduced dose levels. By comparison of the obtained dark-field images we could show which requirements an x-ray dark-field lung imaging setup has to fulfill. Our results give an idea of designing a purpose-built optimized grating set with relatively large grating periods. This is of great importance since lower technical demands on grating fabrication could enhance the applicability in clinical routine.

2. Materials and methods

2.1. X-ray grating-based phase-contrast and dark-field imaging

Grating-based x-ray imaging provides access to both the imaginary part β and the real part δ of the complex refractive index n of a material

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

In common x-ray imaging the well-known attenuation coefficient $\mu = 4\pi\beta/\lambda$ with λ being the wavelength of the interacting photons, comprises the image information. Using a Talbot–Lau interferometer also the phase shift $\Phi = 2\pi\delta/\lambda$ is accessible. Hence, the full material and structural information, contained in the complex refractive index n , is available. In this work we used three Talbot–Lau interferometers differing by the employed grating sets, which is sketched in figure 1. A standard lab-based setup consists of a conventional medical x-ray tube of low brilliance, two absorption gratings G0 and G2, one phase grating G1 and a flat-panel x-ray detector. The basic concept relies on the Talbot effect (Talbot 1836). The phase grating G1 imprints a phase-shift pattern onto the incoming wavefront. Further downstream, at certain so-called Talbot distances, an intensity pattern with maximum contrast can be measured, which reproduces the periodic structure of G1 (Arrizón and López-Olazagasti 1995, Suleski 1997). Due to the extended focal spot of the x-ray source, a source grating G0 is necessary. This leads to a generation of many mutually incoherent slit sources, such that the resulting intensity patterns, created by each single slit, overlap constructively at the plane of G2 (Pfeiffer *et al* 2006). The detector pixel size is larger than the period of the interference pattern. Hence, the pattern is not resolved. The third grating G2 with absorbing lamellae has the same period as the Talbot pattern and is placed at the position of its appearance. The intensity modulation is sampled by laterally shifting G2 perpendicular to the beam direction and to the grating lines. The G2 grating, therefore, is moved in fractions of its period p_2 . This process is called phase-stepping. At every G2 grating position an image is acquired. It leads to a sinusoidal intensity modulation in each pixel as a function of the phase-step position (Weitkamp *et al* 2005). This phase-stepping curve is acquired for a reference measurement without a sample and for a measurement with sample. The intensity I for different phase-step positions x is described by

$$I(x) = I_0 + A \cdot \sin\left(\frac{2\pi}{p_2}x + \varphi\right). \quad (2)$$

The curve parameters mean intensity I_0 , amplitude A and phase φ are reconstructed for each pixel either by Fourier transform or a least-square fit. The contrast or visibility of the curve is defined as $V = I_0/A$. The obtained parameters of both curves, differentiated by the subindices s and r for sample measurement and reference measurement, respectively, are used to calculate the three mentioned images, namely attenuation Γ , differential phase $\Delta\varphi$ and dark-field Σ :

$$\Gamma := -\ln\left(\frac{I_{0,s}}{I_{0,r}}\right), \quad \Delta\varphi := (\varphi_s - \varphi_r) \pmod{2\pi}, \quad \Sigma := -\ln\left(\frac{V_s}{V_r}\right). \quad (3)$$

The conventional attenuation image reveals the amount of photons absorbed by passing through the sample. The differential phase image describes the first derivative of the phase shift which is added by the sample to the incoming x-ray wave front. Thus, edges are enhanced and differences between light elements get apparent (Fitzgerald 2000). The dark-field image originates from the reduction of contrast in the Talbot pattern. Hereby, a visualization of structures below the spatial resolution of the imaging system can be achieved (Pfeiffer *et al* 2008, Yashiro *et al* 2010).

Additionally, we introduce the normalized scatter image, which follows the definition of the R -value (Wang and Stampanoni 2013):

$$R = \frac{\Sigma}{\Gamma} = \frac{\mu_d}{\mu_a}, \quad (4)$$

where μ_a denotes the absorption coefficient and μ_d the dark-field extinction coefficient (Lynch *et al* 2011). Both coefficients describe a property of the material. While μ_a depends on the chemical composition of the material and the x-ray energy only, the scattering coefficient μ_d in addition depends on the structure size in the material—like alveoli in the lung—and on parameters of the Talbot–Lau setup like the grating periods and grating distances. The normalized scatter image is independent of the thickness of the sample and particularly enhances scattering properties (Ludwig *et al* 2018).

2.2. Sensitivity, correlation length and minimal detectable refraction angle

The differential phase signal can be traced back to the refraction angle α the x-ray wave front experiences by passing matter caused by the gradient of the refractive index decrement δ . The refraction angle α of the x-ray beam is interrelated with the differential phase shift $\partial\Phi/\partial x$ of the x-ray wave caused by a sample (Donath *et al* 2009):

$$\alpha = \frac{\lambda}{2\pi} \frac{\partial\Phi}{\partial x}. \quad (5)$$

The connection to the measured lateral phase shift $\Delta\varphi$ in the phase-stepping curves, referring to Weitkamp *et al* (2005), is given by:

$$\Delta\varphi = 2\pi\alpha \frac{d}{p_T} \quad (6)$$

where d is the distance between the phase grating G1 and the analyzer grating G2 and p_T is denoted as the period of the Talbot pattern, which is equal to the period p_2 of G2.

Donath *et al* (2009) address the influence of the sample-to-grating distance for different interferometer geometries. They derive the dependence of the displacement of the Talbot pattern with respect to the sample's position along the beam path and the refraction angle α by pure geometrical considerations. This leads to the relation

$$\alpha = \frac{p_2}{2\pi d} \frac{l}{l - d_s} \Delta\varphi, \quad (7)$$

in case of a sample-grating configuration, meaning the sample is positioned between the source and the phase grating G1. If the distance between sample and phase grating d_s is assumed as being approximately zero, the original formula of equation (6) is retrieved again. In that special case the interferometer has its maximum angular sensitivity. The angular sensitivity S for an interferometer is according to Donath *et al* (2009) defined as the relation of the measured phase shift of the phase-stepping curve $\Delta\varphi$ and the refraction angle α :

$$S := \frac{1}{2\pi} \frac{\Delta\varphi}{\alpha} = \left(1 - \frac{d_s}{l}\right) \frac{d}{p_2}. \quad (8)$$

Note, that the term *sensitivity* is used ambiguous in literature. In Modregger *et al* (2011), Thuerling and Stampf (2014) and Birnbacher *et al* (2016) angular sensitivity is defined as the minimum resolvable refraction angle

$$\alpha_{\min} = \frac{p_2}{2\pi d} \frac{l}{l - d_s} \sigma_\varphi, \quad (9)$$

where σ_φ denotes the standard deviation of the lateral shift of the interference pattern. It depends on the measured visibility as well as on the photon counts and can be associated with the minimum detectable electron density variation (Modregger *et al* 2011).

The preceding descriptions focus on the analysis of the differential phase image. The angular sensitivity as well as the minimum resolvable refraction angle characterize an interferometer setup regarding the obtainable contrast of small electron density variations. The origin of dark-field signal is treated in several publications (Yashiro *et al* 2010, Lynch *et al* 2011, Revol *et al* 2011, Gkoumas *et al* 2016, Koenig *et al* 2016). In Lynch *et al* (2011) a parameter describing the behavior of the dark-field signal is introduced as autocorrelation distance

$$\xi = \frac{\lambda L_s}{p_2}, \quad (10)$$

with λ the x-ray wavelength and L_s the distance between sample and the analyzer grating G2. However, this formula is valid for samples placed between phase and analyzer grating (grating-sample configuration). In Strobl (2014) the parameter ξ is introduced as correlation length also for the case of a sample-grating configuration where a modified distance

$$L'_s = (l + d - L_s) \cdot \frac{d}{l} \quad (11)$$

is required. Using the distance between sample and phase grating G1 as $d_s = L_s - d$ for a sample-grating configuration the correlation length becomes

$$\xi = \frac{\lambda d}{p_2} \left(1 - \frac{d_s}{l}\right). \quad (12)$$

In Strobl *et al* (2016) the correlation length ξ is also called dark-field length connecting the dark-field value with the real space correlation function and a macroscopic scattering cross section. By varying the correlation length in a significant range of values, it is possible to get a full and quantitative characterization for scattering structures of different size, shape and volume fraction (Strobl 2014, Strobl *et al* 2016). Therefore, an optimization of the setup parameters regarding the correlation length should be considered for different tasks.

Comparing the definition of the correlation length (equation (12)) with the definition of angular sensitivity (equation (8)) by Donath *et al* (2009) and the minimum resolvable refraction angle (equation (9)) one finds

$$\xi = S \lambda \propto 1/\alpha_{\min}. \quad (13)$$

Table 1. Grating distances for each setup. The distances source-sample and source-detector were held constant at 83 and 193 cm, respectively, leading to a magnification of $M = 2.3$.

Setup	l (G0 to G1) (cm)	d (G1 to G2) (cm)
A	125.0	12.3
B	97.0	40.3
C	97.0	72.8

Table 2. Grating parameters for the three setups. The duty cycle is defined as grating bar width to period. All gratings are made of gold.

Setup	A			B			C		
Gratingtype	G0	G1	G2	G0	G1	G2	G0	G1	G2
Period(μm)	24.39	2.19	2.40	11.54	3.39	4.80	13.31	5.71	10.00
Dutycycle	0.50	0.66	0.50	0.50	0.50	0.50	0.66	0.30	0.50
Gratingheight(μm)	150.00	4.40	90.00	270.00	6.40	180.00	200.00	6.30	200.00

Hence, there is a connection between the minimum resolvable refraction angle and sensitivity, visible in the differential phase image, and the dark-field image, which is represented by the correlation length.

2.3. Specification of the compared setups

The measurements of an *ex vivo* porcine lung were performed with a Siemens MEGALIX CAT Plus 125/40/90-125GW medical x-ray tube using a tungsten anode with focal spot size of 0.3 (IEC 60336), respectively 0.4 mm $\times$ 0.65 mm (H $\times$ V) at 15% of the maximum value. The used x-ray flat panel detector was a PerkinElmer Dexela 1512 with 74.8 μm pixel pitch running in 2×2 binning mode for processing a faster read-out resulting in a 150 μm pixel pitch. We used three different grating sets while the periods of the analyzer grating G2 varies from 2.4 μm (grating set A) and 4.8 μm (set B) to our optimized setup (Rieger *et al* 2017) with a comparatively large period for G2 of 10 μm (set C). The parameters for each setup are summarized in table 1 for the distances and in table 2 for the grating properties. The source-detector distance was kept constant at 193 cm. Also, the sample position remained unchanged at a distance of about 83 cm to the x-ray source. Hence, the magnification for all measurements was $M = 2.3$. This yields an effective pixel size of about 65 μm in the sample plane for the 2×2 binning mode. We applied an 80 kVp x-ray spectrum, filtered by 0.3 mm copper in order to suppress low x-ray energies. The images for grating set A were acquired for each phase-step with 3.6 mAs and the images for set B and C with 3.0 mAs. Overall, 12 phase-steps were performed. The applied dose (air kerma) was about 0.98 mGy for grating set A, 0.22 mGy for grating set B and 0.32 mGy for grating set C. The dose has been measured during a free-field measurement in sample plane by a DC300 ionization chamber of IBA dosimetry. The gratings for each setup have an area of about (5 $\times$ 5) cm^2 . The measured region in the sample plane is reduced in accordance to the magnification factor. The largest area of (21 $\times$ 26) mm^2 in the sample plane is covered by grating set A, while grating set B covers about (13 $\times$ 28) mm^2 and grating set C covers a field of view of about (22 $\times$ 20) mm^2 .

All gratings were fabricated by the Karlsruhe Nano Micro Facility/Karlsruhe Institute of Technology (KNMF/KIT) using deep x-ray lithography (Meyer and Schulz 2015).

2.4. Sample preparation

The freshly dissected porcine lung was provided by the local slaughter house. For the particular purpose of our studies, no animal has been harmed. The lung has been fixed in an artificial thorax (Biederer and Heller 2003). The artificial thorax represents a chest phantom with shape and size of an actual porcine thorax. The half shells were closed hermetically while the trachea was connected with the environment via an inserted tube. By evacuating the inner pleural space of the chest phantom during the whole measuring time, the lung has been passively inflated inside the entire chest phantom. The bottom side is equipped with the shape of an artificial diaphragm.

3. Results

3.1. Visibilities

The three setups are optimized for different spectra. A wave-field simulation (Ritter *et al* 2014) is used to calculate the expected reference visibilities V_r for each grating set at different monochromatic photon energies. The resulting visibility spectra are shown in figure 2 on the left-hand side. The energy spectrum for 80 kVp (provided by Siemens.com (2019)) which includes a 0.3 mm copper filtration and the detection efficiency of 600 μm CsI is overlaid to the same plot. The visibility spectra of setup B and C match the course of the spectral density distribution quite well, while setup A is more suitable for a spectral density distribution of lower peak voltage. Setup A demonstrates a visibility spectrum distributed around lower energies with a maximum visibility of 40%

at 40 keV, dropping quickly to small visibility values at higher energies. The energy range with visibility values higher than 20% is comparatively narrow. Setup *B* represents a grating set optimized for higher energies. Over a large range of higher energies a sufficient reference visibility is gained. However, the maximal obtained visibilities are in comparison with the other grating sets rather low. Setup *C* reaches a maximum of 67% at 45 keV and achieves high reference visibilities over a broad range of energies. Hence, the optimized grating set is usable for lower and for higher energy spectra.

In figure 2 on the right-hand side the actual measured reference visibilities in each pixel for the applied 80 kVp spectrum for all three grating sets are depicted as visibility maps. The recognizable features, showing reduced visibility, occur due to grating defects. The variation in reference visibility over the whole field of view is caused by inhomogeneities of the gratings. As the visibility spectra have already shown, grating set *A* is more optimized for lower energy spectra, suitable for e.g. mammography, which has been demonstrated with a comparable setup in Michel *et al* (2013). Thus, the averaged reference visibility $V_{\text{mean}}^A = (9.0 \pm 0.9)\%$ for the filtered 80 kVp spectrum is rather low. The error is given as standard deviation of the measured visibility in all detector pixels. Grating set *B* was built as a high energy setup for the implementation of a Talbot–Lau interferometer in a C-arm setup (Horn *et al* 2018). Here, it leads to a reference visibility of $V_{\text{mean}}^B = (17.5 \pm 2.4)\%$. Rieger *et al* (2017) investigated the influence of different grating parameters such as duty cycle and grating bar height by wave-field simulation and experiment. A duty cycle of 0.3 for the phase grating G1 proved to raise visibility in some cases as shown in Rieger *et al* (2016). For the best combination of grating parameters gained from these studies we built an optimized high-energy setup, which is here used as third grating set *C*. In Horn *et al* (2017) the setup was already applied to knee measurements at 70 kVp, with the only difference of employing a G0 grating with a duty cycle of 0.5 instead of 0.66, resulting in an averaged visibility of 28%. In this work, applying a higher energy spectrum of 80 kVp, the obtained visibility for the optimized setup *C* shows homogeneous values over all pixels distributed around the mean value of $V_{\text{mean}}^C = (26.1 \pm 1.1)\%$.

3.2. Porcine lung images

As mentioned in section 2.3 only small fields of view are covered at the sample tray surface due to the limited size of the gratings. Therefore, a large number of single images hat to be acquired to cover the porcine lung. After extracting the attenuation, differential phase and dark-field images, the single image tiles were stitched together. A correction of phase drifts in the reference phase over the measurement time were applied to the differential phase images based on Kppler *et al* (2014). The attenuation and dark-field images were not filtered afterwards to not influence the following analysis. Using the same focal spot size, the same detector pixel size and the same magnification factor the effects discussed in Koenig *et al* (2016) do not influence the obtained dark-field values. Thus, we concentrate our analysis on the parameters correlation length ξ and reference visibility V_r with respect to the different grating and geometry parameters.

Figure 3 shows the resulting attenuation, differential phase and dark-field images of the porcine lung for each grating set. The attenuation images are adjusted to the signal strength of the lung. In the bottom part of the images the artificial diaphragm is visible as rounded shape. The heart consists of muscle tissue and blood, while the lung is mainly composed of air filled alveoli. Thus, the incoming x-rays are much less attenuated by the lung tissue than by the denser heart tissue. On the contrary, the dark-field image especially emphasizes the lung tissue. For a quantitative comparison of the contrast between lung tissue and background for dark-field and attenuation, the Michelson contrast C_M is evaluated. It is defined as:

Figure 3. Attenuation Γ (top), dark-field Σ (middle) and differential phase image $\Delta\varphi$ (bottom) of a porcine lung in an artificial thorax obtained with grating set A (left), B (middle) and C (right).

$$C_M = \frac{\mu_{\text{sig}} - \mu_{\text{back}}}{\mu_{\text{sig}} + \mu_{\text{back}}} \quad (14)$$

where μ_{sig} and μ_{back} denote the mean values of the considered signal and background region. In table 3 the calculated Michelson contrast for attenuation and dark-field is listed for each setup. The Michelson contrast obtained for the dark-field images is much higher than for the attenuation image. The heart does not consist of a porous microstructure and appears almost black in the dark-field images, which means no dark-field signal occurs unless it is partly covered by lung tissue. The differential phase image in particular enhances the edges of the heart and larger vessels. The lung region, however, just looks kind of noisy in the differential phase image and shows no strong contrast to the surrounding tissue. In this publication the focus lies on the comparison of the dark-field images, thus, attenuation and differential phase image will not be considered in detail any further in the following.

Table 3. The Michelson contrast C_M is calculated for attenuation Γ and dark-field Σ for the region of interests shown in figure 6 as black rectangle (lung) and white rectangle (background). The Michelson contrast is much higher for the dark-field values than for the attenuation values. The error of the averaged Michelson contrast values are in the order of 10^{-3} and thus, has been omitted.

Setup	$C_M(\Gamma)$	$C_M(\Sigma)$
A	0.33	0.88
B	0.34	0.96
C	0.33	0.97

Table 4. The mean dark-field values for the region of interest shown in figure 6 as black rectangle and the calculated correlation lengths for each setup are displayed. A low correlation length results in a low dark-field signal. The error of the averaged dark-field values is in the order of 10^{-3} and thus, has been omitted.

Setup	Dark-field Σ	Correlation length ξ (μm)
A	1.57	0.62 ± 0.03
B	1.98	1.31 ± 0.06
C	1.94	1.14 ± 0.05

Because the very same lung was used for all measurements, a shrinking of the lung volume is visible from C to B to A. The first measurement with grating set C started directly after the passive ventilating of the full lung volume. The acquisition of the images shown in figure 3 took about 90 min. Between two measurements a break of about two hours was needed for the exchange of the grating sets. Although the vacuum was maintained over the whole time, the inflated lung lost air over several hours from the measurement with grating set C to set A. This effects in a shrinking of the left and right lung, visible in size and shape of the complete porcine lung. In figure 4 a line plot through the lung and heart region for the dark-field values is shown. While the course of the dark-field signal is similar for grating set B and C, it differs clearly for grating set A. The contrast between lung and heart tissue is much lower. Nevertheless, the noticeable features, like small dips and peaks in the lung and heart tissue are still identifiable.

In figure 5 the thickness independent normalized scatter image is depicted. Heart and lung are even better distinguishable in the normalized scatter image $R = \frac{\Sigma}{\Gamma}$ than in the dark-field image Σ alone. Additionally, the image comprises also information about the course of blood vessels, obtained by attenuation.

3.3. Correlation lengths

There are two parameters which are often discussed in Talbot–Lau imaging aiming at image quality: visibility and sensitivity. The former is addressed in section 3.1, the latter will be treated in the following by looking at the correlation length as introduced in section 2.2 for the x-ray dark-field. Referring to equation (13), sensitivity is directly connected to the correlation length by the wavelength.

The exact specification of a correlation length ξ by equation (12) is hardly feasible as we are using a polychromatic x-ray spectrum. To get a value for the correlation length, anyway, $\lambda = 23$ pm is chosen which is the mean wavelength of the filtered 80 kVp spectrum including the detection efficiency, gained from the simulated course in figure 2. Further on, the distance from different sample regions to the phase grating varies up to 20 cm depending on the thickness of the lung. Thus, a mean distance of the selected region of interest has been chosen for the calculation of the correlation length. However, there is no strong influence of these aspects on the following comparison of the dark-field images, because they were acquired with the same spectrum and the same lung region at the same G0-sample-distance is analyzed.

Setup A has a larger sample to G1 distance than the other two setups. In addition, the ratio of Talbot distance and grating period G2 are similar for setup B and C and differs more for setup A. Thus, the resulting correlation lengths are quite similar for setup B and C with $\xi = (1.31 \pm 0.06)$ and $\xi = (1.14 \pm 0.05) \mu\text{m}$, respectively, while the correlation length for setup A yields $\xi = (0.62 \pm 0.03) \mu\text{m}$. In table 4 the dark-field values obtained for the regions marked in figure 6 as black rectangle are shown together with the correlation length values for each setup. It is obvious that a small correlation length leads to a smaller dark-field value caused by the lung tissue. The presented dependence is observable over the whole lung region in the dark-field images in figure 3 as well as in the normalized scatter images in figure 5.

3.4. Contrast-to-noise ratios

In the following the contrast-to-noise ratios are compared. Here, the contrast-to-noise ratio (CNR) is denoted as

$$\text{CNR} = \frac{|\mu_{\text{sig}} - \mu_{\text{back}}|}{\sigma_{\text{back}}} \quad (15)$$

with μ_{sig} and μ_{back} the mean values of the considered signal and background region and the appropriate standard deviation for the background region σ_{back} . The CNR values are calculated for the regions of interest marked as black (lung tissue) and white (background) rectangles in the dark-field images above the graph in figure 6. The averaged contrast-to-noise ratios normalized by the square root of dose $\text{CNR}_d = \text{CNR} / \sqrt{D}$ are plotted for each setup for the dark-field in figure 6. Setup *A* leads to the smallest CNR_d , while *C* reaches the highest value.

3.5. Varying dose levels

The thickness independent normalized scatter images in the x-ray dark-field images are quite high for lung tissue. Thus, the question arises how high the applied dose has to be in order to receive diagnostic relevant information from the dark-field images. Actually, our data shows no distinctive lung diseases and the results are restricted to this specific study imaging a porcine lung in a chest phantom. Hence, our statements give rather a rough estimation of the expected order of magnitude for required dose levels in x-ray dark-field lung imaging. However, we want to visualize the influence of the investigated grating sets on the behavior of contrast-to-noise ratio to dose.

On this account, the raw data obtained by setup *A* and by the optimized setup *C* were analyzed once again for reduced dose levels by using less phase-steps for the image extraction. As the CNR_d value for setup *B* lies between the values for setup *A* and *C*, this analysis has been omitted for setup *B* for clarity. Since three phase-steps are theoretically sufficient for getting the necessary parameters of the phase-stepping curve (Weitkamp *et al* 2005), a reconstruction with one quarter, one third, and one half of the full dose of 0.32 mGy air kerma were done for setup *C*. In the case of setup *A* three single acquisitions of the lung were performed. Therefore, the extraction of dark-field images at lower dose levels starting from $\frac{1}{12}$ of the full applied dose of 0.98 mGy air kerma are feasible.

Figure 6. The normalized contrast to noise ratios CNR_d are shown for the grating sets A, B and C. The dark-field images on top show the selected regions of interest marked with black (lung) and white (background) rectangles for the calculation of the averaged CNR_d displayed in the graph. The error of the CNR_d values is neglectable and thus, has been omitted.

Actually, the reconstruction with only three phase-steps lead to moiré artifacts for setup A and for this reason, was omitted in the subsequent analysis.

In figure 7 the CNR values for setup A (blue curve) and C (red curve) are plotted over the applied dose and show the typical square root behavior regarding the dose. Grating set A reaches a lower normalized contrast to noise ratio of $CNR_d = 39 (\text{mGy})^{-0.5}$ than grating set C with $CNR_d = 154 (\text{mGy})^{-0.5}$. Nevertheless, a strong dark-field signal above the noise level occurs for the lung tissue in both cases, even at a lower dose. The data at the lowest reconstructable dose level for setup A still contains sufficient information, which is visible in figure 7 by comparing the shown images at lowest and highest applied dose. The lower dose, of course, results in a higher noise level. Nevertheless, in our study, heart and lung region are clearly separable and also the morphology of the lung is preserved at reasonable dose regarding clinical applications.

4. Discussion

We acquired images of a porcine lung by using different grating sets with the focus on the comparison of the obtained x-ray dark-field images. Firstly, we demonstrated that for lung tissue a significantly higher Michelson contrast is obtained by dark-field than by attenuation valid for all used grating sets. For that reason, x-ray dark-field imaging is a very promising method for an improved diagnosis of lung diseases, as already shown in many publications.

Additionally, we proposed the normalized scatter image as an alternative depiction of lung images with regard to diagnostic purposes. It comprises thickness independent information about scattering properties as well as attenuation properties. Hence, in further studies an analysis of the normalized scatter image regarding lung diseases should be considered.

While the dark-field image of the porcine lung is quite similar for setup B and C, it differs clearly for setup A. The dark-field signal of the lung tissue is lower for setup A. Simultaneously, the image shows a higher dark-field for the heart tissue, visible in the line plot in figure 4. This comparatively lower contrast between lung and heart for setup A could be explained by the spectrum energies the grating set is optimized for. As seen in the simulated visibility spectrum for setup A (figure 2) the visibility drops for higher energies, quickly. Thus, beam hardening effects carry more weight. The heart region tends to cut the lower part of the spectrum. The measured visibility is a weighted average of the contributing monoenergetic visibilities. Thus, the spectrum weighted visibility decreases for setup A in the heart region due to the missing spectrum parts, which would contribute to higher visibility values. This results in a stronger dark-field signal in the heart region. The reduced dark-field in the lung region, on the contrary, can be explained by the low correlation length (section 3.3) which is mainly caused by the large distance from the porcine lung to the phase grating.

The connection of correlation length and dark-field also influences the obtained CNR_d values depicted in figure 6. In addition, a low visibility, which results in higher noise occurrence in dark-field images (Revol *et al* 2010), also contributes to the CNR_d results. Because setup C reaches the highest reference visibility and shows a high contrast between lung tissue and background, it leads to the highest CNR_d . The lowest CNR_d is gained for setup A, featuring the lowest visibility and the lowest dark-field for the lung tissue. The minimal higher contrast retrieved for setup B in comparison to setup C carries less weight compared to the influence of lower visibility causing a higher standard deviation in the considered regions of interest due to noise.

Still, all setups gain quite high CNR_d values for lung tissue. In this regard, the extraction of dark-field images for different dose levels comparing the grating sets has been evaluated. For setup A the lowest $\text{CNR} = 13$ is reached for a dose of about 0.1 mGy, where the morphology is sufficiently preserved. The obtained CNR values for setup C are much higher than for setup A. The maximum applied dose of 0.32 mGy, here, leads to a $\text{CNR} = 85$. Hence, a dose of 5 μGy (resulting in an estimated $\text{CNR} = 11$) is regarded as sufficient to image a porcine lung in an artificial thorax with our optimized setup C. Note, that the finding is restricted to the presented study since a human body undoubtedly requires a higher amount of dose. However, in Hauke *et al* (2018) a reader study was performed to evaluate the impact of dose reduction regarding diagnostics. The authors mentioned 0.3 mGy air kerma as sufficient for a full body imaging of a living pig, while the results were obtained with a grating set similar to grating set B. Hence, our results indicate, that an optimized setup like our presented setup C featuring high visibility and correlation length could further reduce the necessary dose level. However, the recognizability of conspicuous features in noisier dark-field images should be evaluated in more details in further studies on human bodies.

In this study, small fields of view were acquired in a time consuming measuring process. The single tiles were then stitched together in a post-processing step. Thus, a grating set optimized in particular for lung imaging may be designed as a scanning device for faster acquisition and a larger field view regarding the implementation in a clinical routine. The aspect of an extended medical x-ray imaging system has already been published for different approaches (Astolfo *et al* 2017, Bachche *et al* 2017, Gromann *et al* 2017a). Furthermore, in a living body moving artifacts induced by heart beating or breathing during the phase-stepping procedure could be problematic. Here, single-shot moiré imaging, which enables a faster acquisition, already showed promising results for lung imaging (Seifert *et al* 2018).

Finally, our results show that lung imaging is feasible as long as visibility and correlation length are sufficiently high. These findings are not directly restricted by the need of small grating periods because x-ray dark-field lung imaging has not to be sensitive to small structural changes in a very localized manner. In this regard, we demonstrated that high contrast-to-noise ratios are achievable with the presented optimized setup C, featuring a relatively large analyzer grating period of 10 μm and a moderate setup length of about 2 m. Large grating periods are an advantage regarding the fabrication of the absorption gratings with high aspect-ratios. These are necessary for imaging a human thorax at typical energies of 60–90 keV. Hence, it is more probable that such gratings can be produced for a clinical lung imaging setup.

5. Conclusion

X-ray dark-field imaging has great potential for the clinical applicability regarding lung imaging. In this publication we compared three different grating sets regarding x-ray dark-field imaging of a porcine lung. The grating periods of the analyzer grating G2 varied from 2.4 to 4.8 and 10 μm . X-ray tube, magnification of the sample and the detector were the same for all measurements. Thus, the compared results of the dark-field images

only depend on the interferometer specifications. Setup C, featuring the largest analyzer grating period, is the result of an optimization procedure. It leads to an averaged reference visibility of 26% and a correlation length of $\xi = (1.14 \pm 0.05) \mu\text{m}$ for a 80 kVp x-ray spectrum. The lung tissue causes a strong dark-field signal with the highest normalized contrast-to-noise ratio by using setup C compared to setup A and B.

For the presented study a dose of 5 μGy air kerma is regarded as sufficient in order to preserve the occurring lung signatures acquired by grating set C featuring the highest visibility and a high correlation length. The results are an indication of how little dose is needed for x-ray dark-field imaging of lung tissue.

In conclusion, our study demonstrates that a sufficiently high dark-field signal for healthy lung tissue is obtainable with larger grating periods at moderate grating distances. This simplifies the design of an x-ray dark-field lung imaging setup. Lung imaging needs high x-ray energies which require relatively thick analyzer gratings G2. As the aspect ratio for grating thickness to grating period is limited by the production process our solution with a relatively large G2 grating period of 10 μm shows the right way to clinical lung imaging.

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Disclaimer

The system presented in this paper is a research device and not commercially available.

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