

Point-by-point response to the reviewers

Revised manuscript NCOMMS-13-09247-T

The comments from the reviewers are quoted in *italic*, whereas the revised article parts are reported in upright font in indented sections.

Reviewer #1

I could not find a significant advance in this work. X-ray Talbot-Lau interferometers with high-energy x-rays have been already reported (Ref. 18-20, 23, D. Stutman et al., Appl. Opt. 49 (2010) 4677 etc.). The authors mention that the edge-on- illuminated grating interferometry breaks the current limitations of x-ray phase-contrast imaging, but I don't think that there is clear evidence showing that the authors' method is much more promising than the methods reported in the previous papers. If the authors want to show that the edge-on-illumination method is by far the most promising for high-energy and large-field-of-view x-ray phase imaging, I think that the authors have to quantitatively compare the method with those previously reported in terms of the total exposure time, spatial resolution, signal-to-noise ratio, and so on, and show that the authors' method is much better than the others.

Stuntman et al. present a method which increases the effective aspect ratio of the gratings by slightly rotating them along an axis perpendicular to the propagation direction. However, his method has the major limitation of not being compatible with divergent geometries. As a result, his interferometer will show a high visibility, although still limited compared to what we can achieve in theory, but its horizontal field of view will be strongly limited in case of divergent beams, as commonly found in any table-top device. Our solution, on the other hand, solves both issues at the same time, and therefore we consider this as a significant improvement with respect to Stuntman's work. Moreover, the cited experiments were performed on a source with 60 kVp, which is significantly lower than the 160 kVp of our source and the 100 keV used as the design energy for our interferometer. Reviewer #1 further cites other related works which, however, were carried out either in much lower energy range or under very different imaging conditions, thus preventing a meaningful comparison.

Reference 23 reported images taken at 30 and 60 keV, reference 20 also has a design energy of 47.9 keV. Finally, references 18 and 19 present Talbot interferometry at 82

and 123 keV respectively, but only the first result is published on a peer reviewed journal, and both experiments were performed at the ESRF synchrotron, with a monochromatic and coherent beam that is incomparable to a conventional tube. In order to emphasize this enormous difference between synchrotron sources and lab sources, the title has been changed to “X-ray phase-contrast imaging at 100 keV on a conventional source”.

In order to address the concerns of reviewer #1, the short review of the previous results in the introductory paragraph has been updated:

The vast majority of phase-sensitive techniques, including crystal analyzer based [5, 6] or interferometric [7, 8] methods rely on X-ray beams of high spatial and temporal coherence, which is available only at synchrotron sources. Inline phase contrast [9–11] and Talbot interferometry [12–14] need high spatial coherence but are available on polychromatic microfocus sources. Phase-contrast imaging using X-ray beams of low temporal and spatial coherence such as conventional low-brilliance X-ray tubes have been demonstrated with coded apertures [15] and Talbot-Lau interferometry [16]. Analyzer-based systems have been recently extended to tube sources [17, 18] but only at energies up to the tungsten K_α line at 60 keV. In addition to phase sensitivity, analyzer-based and Talbot interferometry also provide (with different retrieval mechanisms) information about the integrated local small angle scattering power from microscopic density fluctuations in a specimen [19]. This signal is known under the name of dark-field, scatter or visibility reduction contrast. High-energy Talbot interferometry has been reported so far using a synchrotron source at nominal energies of 82 keV [20] and 123 keV [21]. Using a low-brilliance X-ray tube, Talbot-Lau interferometry was applied so far at 60 keV mean energy [22]. Medical imaging applications may benefit from phase contrast at higher energies: chest or abdominal radiography or CT require an acceleration voltage between 100 and 150 kVp. Other potential applications are homeland security or chip failure analysis, which require high energies for the visualization of materials of high density and atomic number.

Furthermore, the authors mention that the results in Fig. 3 show the benefit of the phase nature of the image, but I think that the authors should provide a more detailed explanation about the contrasts in the images because the contrast of soldering points underneath the resistors should not be reduced in the differential attenuation image for monochromatic x-rays. The authors should explain quantitatively why the contrast is reduced. Otherwise, the authors’ assertion is suspicious.

A paragraph has been added to discuss the different beam hardening behaviour of the absorption and differential phase image:

In the attenuation image, the contrast of the soldering points of the integrated circuit is reduced underneath the resistors, while in the phase image, they can clearly be identified. The reduced contrast of the soldering points in

the absorption image is due to beam hardening. The spectrum impinging on these soldering point is hardened by the resistors in the upper layer, resulting in lower absorption contrast. Due to the weaker energy dependency of phase shifts ($1/E$ compared to $1/E^3$), phase-contrast images are less sensitive to beam hardening [31], which explains the lower contrast reduction of the soldering points underneath the resistors in the phase image of the chip. This result shows the benefit of the phase contrast in high-energy X-ray imaging, which may be useful to identify flaws in multilayered structures such as electronic chips.

Reviewer #2

However, this solution comes with significant drawbacks in terms of very limited fields of view 3 cm horizontally, a single detector pixel in the vertical direction), which at the moment seem hard to overcome.

There is no fundamental limitation on the horizontal field of view in our approach. On the contrary, our solution actually solves precisely this issue, by easily matching the spherical wave front with the curved structures. Our approach removes any limitation to the horizontal field of view which would arise due to the large beam divergence. In addition, curved gratings can be easily stitched to cover an even larger field of view, if necessary.

With our scanning solution, the limitation of the vertical field of view does not come at the expense of an increased dose. A similar scanning technique is already commercially offered in X-ray mammography systems, like the MicroDose instrument of Philips, with a significant reduction of the scattered radiation. We discussed this issue and amended the text accordingly.

Radiographic 2D imaging can be obtained by scanning the sample or a thin fan beam. The scanning technique has been demonstrated to deliver less dose than the conventional approach based on the illumination of a large area. In digital mammography, for instance, where dose is a critical issue, Philips' MicroDose system combines a scanning approach with an highly collimated fan beam [27]. Thanks to the high collimation, the dose deposited on patients has been reported to be significantly lower than with other instruments based on the illumination of a large area detector [28].

Moreover, in the methods section the authors talk of a 5 % visibility, which is even lower than that of the quoted papers by Pfeiffer's group (refs 18, 19), which, at least nominally, reach even higher energies (123 keV). Hence, the reduction in field-of-view does not seem to be counterbalanced by significant improvements in visibility. This is also supported by the relatively poor quality of the differential phase image compared to the derivative of the absorption image, where the only advantage seems to be the visibility of the soldering

points beneath the resistors (primarily due to the fact that these do not produce area contrast in the DPC image), while everywhere else the contrast of the differentiated absorption image seems to be higher.

We would like to remind to the reviewer #2 that our data have been obtained on a commercially available X-ray tube, while the cited experiment of Pfeiffer's et al. has been carried out at a third generation synchrotron source, where notably unsurpassed beam conditions can be created which are far from what one can expect in real life (i.e. with conventional X-ray tubes). And, even if one would like to still carry out this (unfair) comparison, we should mention that our experiment is the first measurement of its kind with the first generation of gratings made according to our innovative design. Pfeiffer's team uses gratings obtained after almost a decade of development and, despite this and the use of a synchrotron, they are not really further than us while they still carry the intrinsic limitation of a limited grating height. We are well aware that the quality of our images has still to be improved, but here we are presenting the first experiments with edge-on grating illumination: we describe its great potential but also mention its (temporary) limitations.

Finally, the novelty of the result is diminished by previous demonstrations that high energies in phase-contrast x-ray imaging could be reached by other methods (e.g. Ignatyev et al JAP 110 (2011) 014906), albeit in that case image quality seems to be lower.

Reviewer #2 admits that in comparison with a coded-aperture based experiment at 100 kVp (Ignatyev et al.) our images (taken at 160 kVp) are better, which we of course appreciate.

Reviewer #3

An extended object is imaged by axial scanning, which results in very long exposure times due to phase stepping. The legend of Fig. 3 indicates that one image line of 0.1 mm width is acquired in 6 min. The authors admit this situation in the last sentences of the manuscripts without giving a convincing solution to the problem.

This is indeed an issue, as the exposure time is mostly affected by the low visibility. The manuscript was amended to include a more detailed discussion of our plans to reduce the exposure time. We mention now that raising the visibility to 15 %, a value already reached in lower energy experiments and in some sections of our gratings, would immediately cut the exposure by almost an order of magnitude:

The long exposure times are mostly constrained by the low average visibility of the gratings (5 %). The exposure time was chosen in order to get a low noise in the differential phase image. The signal-to-noise ratio (SNR) is proportional to the visibility and the square root of the exposure time [33]. This

implies that the exposure times can easily drop by an order of magnitude as these gratings become comparable in quality to those developed in the last ten years. Smaller regions of these gratings actually exhibit a visibility up to 14 % already, indicating that this goal is reachable as the fabrication becomes more reliable and uniform.

The authors suggest that the only imaging methods that can be used with conventional x-ray sources are the in-line phase contrast technique and Talbot interferometry. They fail to mention that analyzer-based imaging systems with x-ray tube sources have been built and successfully used for imaging rather large biological objects. The current exposure times are shorter or comparable to those of the present work, but there are clear indications how the exposure times in x-ray tube based ABI can be reduced by an order of magnitude or more. On the other hand, the upper limit of photon energy is that of the tungsten Kalpha line, 60 keV. For references, see Nesch et al.(2009), Rev. Sci. Instrum. 80, 093702, and Parham et al.(2009), Acad.Radiol. 16, 911-917.

We thank Reviewer #3 for pointing out this issue. We amended the text accordingly, discussing specifically the cited analyzer-based imaging experiment. In particular, we highlight that the mentioned ABI investigation was carried out at 60 keV, far below our nominal energy of 100 keV. We are also not aware of any ABI operated at energies higher or equal to 100 keV on conventional X-ray sources.