Phase contrast mammography: a novel diagnostic tool for breast imaging

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Purpose

Phase-contrast and scattering-based x-ray imaging are known to provide additional and complementary information to conventional, absorption-based methods [1,2].

Differential phase contrast imaging using grating-interferometer is a promising tool to revolutionize the conventional approach to medical imaging because it can provide three different contrasts simultaneously and works well with conventional X-ray tube [3,4].

In our previous study, we demonstrated that those additional information can provide valuable and yet not accessible technique need to be evaluated statistically [5].

In this work, we present the results of a multicenter, international reader study aiming at the evaluation of the clinical relevance of phase contrast mammography [6].

Methods and Materials

Physical background

Differential phase contrast (DPC) imaging using grating interferometer can generate three different contrasts simultaneously: the conventional absorption contrast, different phase contrast and small-angle scattering contrast. A demonstration of the three contrasts is shown in Figure 1.

The principle of the grating interferometer for DPC imaging is illustrated in Figure 2. Briefly speaking, the system is composed of an X-ray tube, a three-grating interferometer, and a 2D detector. During the data acquisition, one of the gratings is moved perpendicular to the grating lines within at least one gratings period (phase stepping approach). For each pixel on the detector, a quasi-sine intensity curve is recorded. The AC, DPC, and DFC signals are obtained by an information retrieving algorithm [7] operating on phase stepping curves with and without the object.

Patients
The local institution's ethical review board approved this study, and written informed consent was obtained from all patients. The patients included were 1 male and 32 women, over the age of 18, presenting at the Department of Gynecology, Interdisciplinary Breast Center, Baden, Switzerland between November 2010 and April 2012. They were all with histo-pathologically confirmed breast cancer and/or with breast(s) requiring modified radical mastectomy, and were willing to participate in the study.

**MammoDPC system**

Freshly dissected whole breast specimens were imaged using a Talbot-Lau interferometer equipped with a conventional x-ray tube, namely the MammoDPC system (Figure 3). The interferometer was operated at tube voltage of 40 kVp with mean energy of 28 keV, and current of 25 mA. The details of the system can be found in Ref.5.

**Sample preparing and imaging protocol**

The samples are measured with an imaging protocol as similar as possible to in-vivo situations. Native breast tissue was obtained directly after mastectomy and mounted inside a dedicated, cooled breast-tissue holder designed to provide adequate compression of the tissue compared with the in-vivo situation. Ex-vivo mammograms and MammoDPC imaging were then performed at the hospital and at the Paul Scherrer Institute, respectively. Standard histopathological examination followed the MammoDPC acquisition. All results, including MRI, ultrasound, in-vivo and ex-vivo mammograms, and MammoDPC, were then discussed in regularly-scheduled interdisciplinary meetings, which included radiologists, pathologists, breast surgeons, and physicists. The protocol is illustrated in Figure 4.

The three quantities obtained were combined into novel, high-frequency-enhanced radiographic images and compared to digital mammography images [8].

**Study Design[6]**

Two reader studies were designed involving 33 patients, six international breast radiologists and both conventional and phase contrast enhanced (mammoDPC) mammograms.

The first study directly compares images obtained with our demonstrator in absorption and phase-contrast mode using the same dose. This allows a-priori the removal of
instrument specificities and yields system unbiased images. Cranio-caudal (CC) and anterior-posterior (AP) views have been evaluated.

In the second study, mammograms obtained with clinically state-of-the-art digital equipment were compared with absorption and phase-contrast enhanced mammograms. Here, only CC views were included to allow a direct comparison between our experimental images and the diagnostic findings of clinical quality.

Dedicated questionnaires for the two reader studies were prepared including eight questions for study 1 and twelve questions for study 2, each question with graduated, ordinal answers, allowing a statistical analysis. All the reported data are supported by histopathological findings as the ground-truth.

Statistical analysis

Wilcoxon signed-rank test was used for qualitative analysis of subjective preference score in both reader studies. IBM SPSS Statistics 20 (SPSS Inc., Chicago, IL, USA) was used for descriptives and pairwise comparisons (Wilcoxon Signed Ranks Test) of image types.

For all statistical analyses, a two-tailed p<0.05 was considered to indicate a statistically significant difference. For reader study 1, Bonferroni-correction was made to consider the 9 comparisons per view, therefore p#0.05/9 # 0.005 resulted to be significant. For reader study 2, two comparisons per question were considered, resulting in p#0.05/2 # 0.025 for significance.

Inter-observer agreement between the readers was calculated by weighted kappa statistics. Stata 11.2 (StataCorp, Lakeway Drive, TX, USA) was used for computation of kappa-values for interreader variability.

Images for this section:
Fig. 1: The three different contrasts of a human hand. (a) The absorption image (conventional radiography); (b) The differential phase contrast image; (c) The small-angle scattering image.

Fig. 2: The principle of grating interferometer. (a) The scheme of the setup for a parallel beam configuration. The phase gratings generate an interference pattern (beam splitter). A sample in front of the phase grating causes a lateral (x-direction) shift of the interference fringes at the position of the absorption grating. The absorption grating is used to analyze the interference fringes and determine this shift which corresponds to the DPC signal. (b) Reference (blue) and object (light red) phase stepping curve (PSC). From these curves the absorption (a0), the phase (#) and a scattering signal (a1) can be calculated.
Fig. 3: The MammoDPC demonstrator installed at Paul Scherrer Institute, Villigen, Switzerland. (a) MammoDPC system with the X-ray source on the left and the breast tissue holder on the right. (b) The Talbot-Lau interferometer consists of three gratings: G0 = 14µm (not visible), G1= 3.5 µm and G2 = 2.0 µm period.

Fig. 4: The imaging protocol for the study.
Results

The results of study 1

In reader study 1 the six breast radiologists directly compared the absorption and mammoDPC images recorded (with the same dose) at our demonstrator.

Statistical analysis reveals the general quality of the mammoDPC images to be significantly superior than the absorption based images (p<0.001).

Sharpness and lesion delineation as well as the general visibility of calcifications were significantly better assessed in mammoDPC than in absorption images (p<0.001).

MammoDPC images resulted in sharper delineation of surface structures when evaluating the periphery of the images (p<0.001).

Superior findings in calcification sharpness were significantly assessed in mammoDPC compared to absorption images (p<0.001), see Figures 5.

The results of study 2

The second study investigated the three types of images for all 33 patients: conventional mammograms (acquired under the clinical setting with a standard digital mammography system), experimental absorption and mammoDPC mammograms acquired with our demonstrator.

Spiculations were significantly better identified in mammoDPC images compared to conventional mammograms (p<0.015), while absorption images obtained with our demonstrator showed to be directly comparable with the clinical data (p<0.076), see Figure 6.

Blood vessel visibility resulted to be lower in mammoDPC and experimental absorption based images, when compared to the mammograms acquired with the clinical system. This result may be explained by the study design, as a certain amount of time elapsed between the clinical and the experimental measurements, possibly affecting the internal redistribution of the remaining blood within the sample.
A summary of the results of study 1 and 2 is given in Table 2.

Images for this section:

<table>
<thead>
<tr>
<th>Evaluated criteria (mammoDPC is superior)</th>
<th>p-value</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>General quality of image</td>
<td>&lt;0.001</td>
<td>2-3</td>
</tr>
<tr>
<td>Sharpness and lesion delineation</td>
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<td>2-3</td>
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<tr>
<td>Delineation of surface structures</td>
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<td>2-3</td>
</tr>
<tr>
<td>Sharpness of microcalcis</td>
<td>&lt;0.001</td>
<td>2-2</td>
</tr>
<tr>
<td>General visibility of microcalcis</td>
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<td>2-3</td>
</tr>
<tr>
<td>Clinical relevant information</td>
<td>&lt;0.001</td>
<td>4-5</td>
</tr>
<tr>
<td>Identification of spiculations</td>
<td>&lt;0.015</td>
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</table>

<table>
<thead>
<tr>
<th>Evaluated criteria (mammoDPC is inferior)</th>
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<tbody>
<tr>
<td>Lower blood vessel visibility in mammoDPC</td>
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<td>More artifacts in mammoDPC</td>
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<tr>
<td>Signs of skin infiltration</td>
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<tr>
<td>Clusters of suspicious microcalcifications</td>
<td>N/A</td>
</tr>
<tr>
<td>Signs for the presence of DCIS</td>
<td>N/A</td>
</tr>
</tbody>
</table>

* p < 0.005 is considered to be significant with Bonferroni-correction.  
* a) Interquartile range.  
* b) 2 being “superior” and 3 being of “equivalent” quality.  
* c) 4 being “11% to 20% superior” and 5 being “1% to 10% superior”.  
* d) This criteria was evaluated in study 2. p<0.025 is significant with Bonferroni-correction.  
* e) p<0.025 is considered to be significant with Bonferroni-correction.  
* f) No significance was found.

**Table 1:** Statistical outcome from study 1 and 2, showing the criteria under which mammoDPC either outperforms or not conventional mammography [6].
Fig. 5: The PC-enhanced mammogram (a) shows better sharpness and microcalcification visibility than Absorption mammogram (b).
**Fig. 6:** Spiculations were much better identified in PC-enhanced mammogram (a) than Absorption mammogram (b).
Conclusion

Differential phase contrast imaging using grating-interferometer is a promising tool to revolutionize breast imaging. Three different contrasts can be provided simultaneously.

An international team of expert radiologists evaluated the potential clinical significance of phase contrast mammography.

The statistical results of the study confirmed that the novel approach yields images with increased clinical relevance compared to conventional digital mammography in general image quality, image sharpness, microcalcifications sharpness and visibility, delineation of surface structure and spiculations identification.

References


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