

## Cumulative Phase Delay Imaging

**Citation for published version (APA):**

Demi, L., van Sloun, R., Wijkstra, H., & Mischi, M. (2016). Cumulative Phase Delay Imaging. In *Proceedings of the 21th European Symposium on Ultrasound Contrast Imaging, Rotterdam, 2016*

**Document status and date:**

Published: 01/01/2016

**Document Version:**

Publisher's PDF, also known as Version of Record (includes final page, issue and volume numbers)

**Please check the document version of this publication:**

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

[Link to publication](#)

**General rights**

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:

[www.tue.nl/taverne](http://www.tue.nl/taverne)

**Take down policy**

If you believe that this document breaches copyright please contact us at:

[openaccess@tue.nl](mailto:openaccess@tue.nl)

providing details and we will investigate your claim.

# Cumulative Phase Delay Imaging

*Libertario Demi<sup>1</sup>, Ruud J.G. Van Sloun<sup>1</sup>, Hessel Wijkstra<sup>2,1</sup>, Massimo Mischi<sup>1</sup>*

<sup>1</sup>*Department of Electrical Engineering, Lab. of Biomedical Diagnostics, Eindhoven University of Technology, the Netherlands*

<sup>2</sup>*AMC University Hospital, Amsterdam, the Netherlands.*

## Introduction

As cancer needs nutrients and oxygen to grow and spread, it triggers angiogenesis and neovascularization. Consequently, there is growing interest in developing imaging modalities able to detect, localize, and visualize these processes. To this end, dynamic contrast-enhanced ultrasound (DCE-US) represents a valuable option. Unfortunately, performing handheld DCE-US is challenging for the breast as, unlike X-ray CT or MRI, DCE-US imaging of the breast is highly operator dependent.

Based on our recent discovery of a new marker for ultrasound contrast agents (UCAs) [1-2], we are currently developing a novel imaging technique named cumulative phased delay imaging (CPDI). CPDI could potentially lead to the development of three-dimensional contrast-enhanced ultrasound computed tomography (3D CEUS-CT), providing a radiation-free imaging modality that enables visualization of the whole breast vascular architecture in 3D. Such an imaging modality would open new horizons for the detection and localization of breast cancer.

## Method

A (positive) cumulative phase delay (CPD) between the second harmonic (2H) and fundamental (F0) component is observable for ultrasound (US) propagating through UCA. This delay is dependent on agent concentration, propagation path length through UCA, pressure field amplitude, and insonating frequency. Most importantly, this delay is absent in tissue, and clearly observable at frequencies (2.5 MHz) and pressure regimes ( $0.05 < MI < 0.2$ ) of interest for clinical application [1-2]. Consequently, variations in the total time delay between 2H and F0 can be exploited to image and detect UCAs.

## Results

Numerical and *in-vitro* studies confirmed the applicability of CPDI for contrast specific US imaging [2-3], with CPDI showing superior capabilities in detecting and localizing UCA, as compared to speed-of-sound and dispersion-based US tomography [3-4]. Furthermore, phantom experiments showed how cavities of different size (filled with UCA and surrounded by tissue-mimicking material), which were down to 1 mm in diameter, could clearly be detected [3] (see Figure 1). CPD image values relate to the measured delay, which is here expressed in cycles/m.

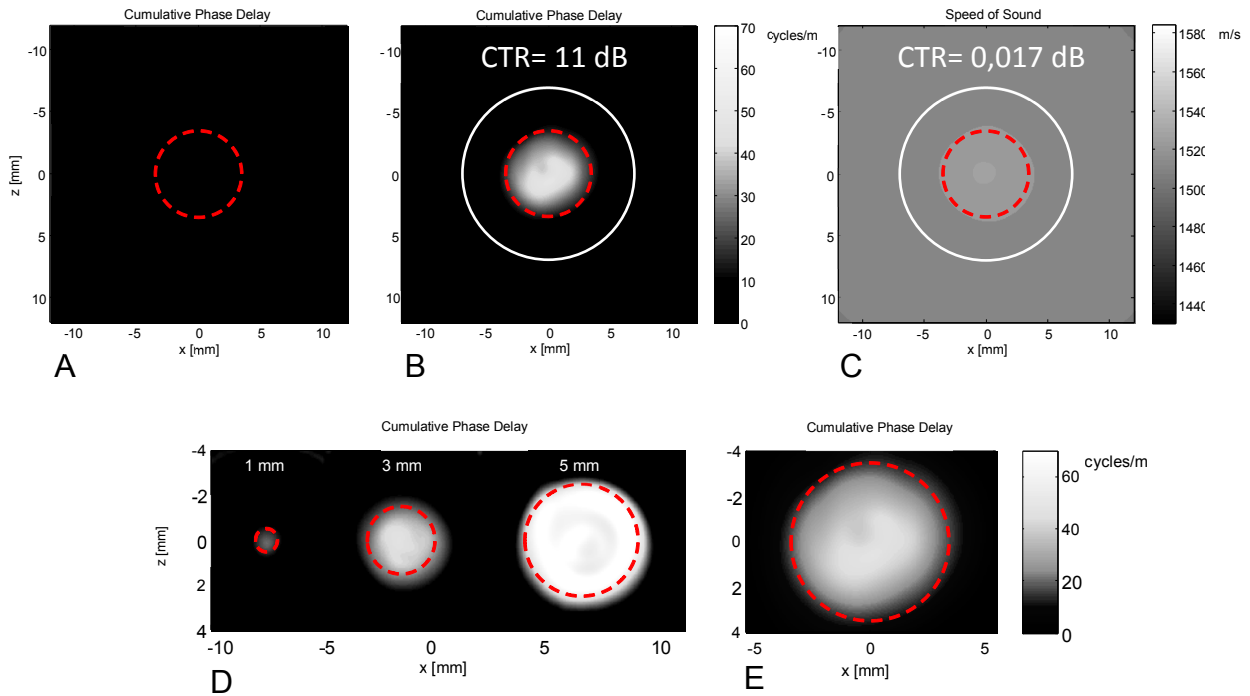


Figure 1: CPD images of a tissue-mimicking phantom containing a 7-mm cavity filled with (A) only saline and (B) SonoVue®. (C) Speed of sound tomographic image as obtained for the same intra-cavity UCA concentration. Contrast to tissue ratio (CTR) values are also shown. CPD images of tissue-mimicking phantoms containing (D) three cavities (measuring from 1 to 5 mm in diameter) and (E) a single 7-mm cavity filled with SonoVue® [3].

## Conclusion and Discussion

CPDI may find relevant application to the development of contrast enhanced ultrasound tomography of the breast aimed at angiogenesis imaging for cancer detection and localization. To this end, investigating the performance of CPDI in estimating UCA flow dynamics and imaging more complex and heterogeneous targets will be the focus of future work.

## References

1. L. Demi, G. Russo, H. Wijkstra, and M. Mischi "Observed Cumulative Time Delay Between Second Harmonic and Fundamental Component of Pressure Wave Fields Propagating Through Ultrasound Contrast Agents", *Proceedings of Meetings on Acoustics 20*, San Francisco, 075002, 2013.
2. L. Demi, H. Wijkstra, and M. Mischi "Cumulative phase delay between second harmonic and fundamental components - A marker for ultrasound contrast agents", *Journal of the Acoustical Society of America*, 136, pp. 2968 - 2975, 2014.
3. L. Demi, R. J.G. Van Sloun, H. Wijkstra, and M. Mischi, "Cumulative phase delay imaging for contrast-enhanced ultrasound tomography", *Physics in Medicine and Biology*, vol. 60, no. 21, pp. L23 L33, 2015.
4. L. Demi, R. J.G. Van Sloun, H. Wijkstra, and M. Mischi, "Contrast enhanced ultrasound tomography by means of the cumulative phase delay between second harmonic and fundamental component", *International Ultrasonics Symposium IEEE*, Taipei, Taiwan, 2015.