Research Methodology

Lecture 4: Review

Professor: Dr. Libertario Demi
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UNIVERSITY OF TRENTO - Italy
Department of Information Engineering
and Computer Science

The Review Process

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L. Demi 2018/19

Basic etiquette

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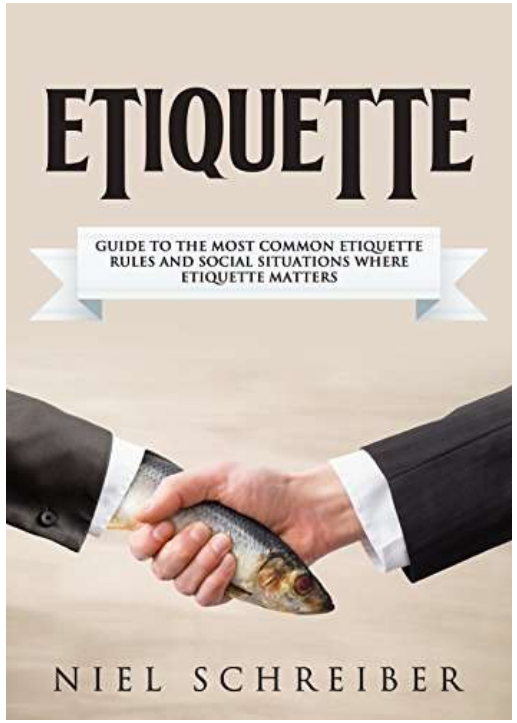
- Read the entire paper before starting the review process



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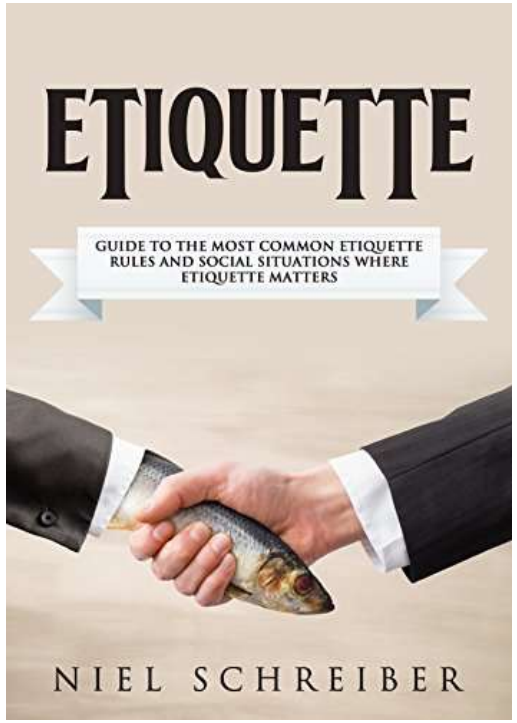

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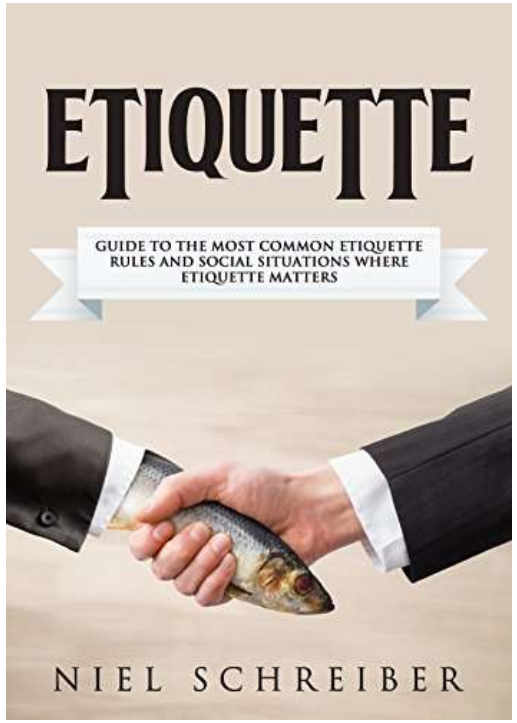

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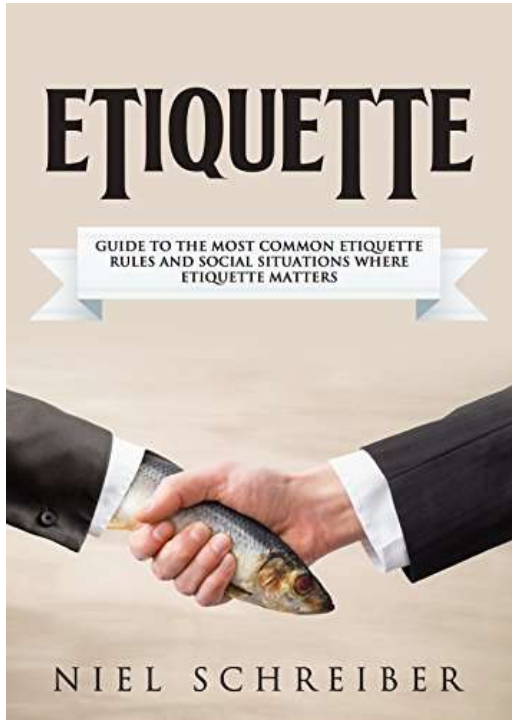

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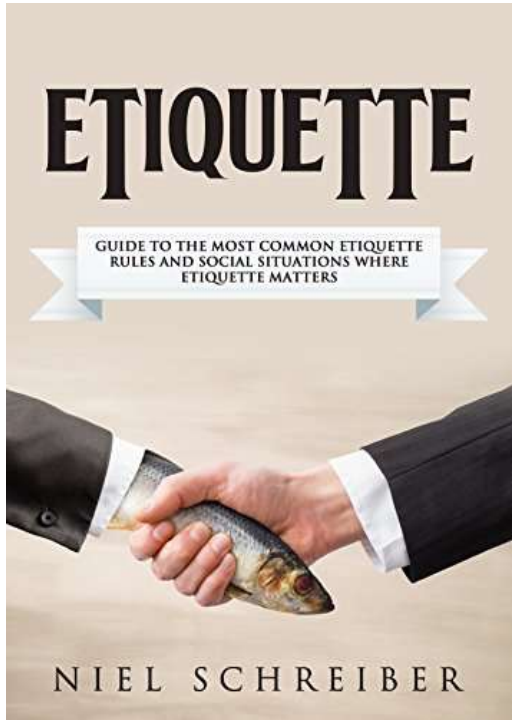

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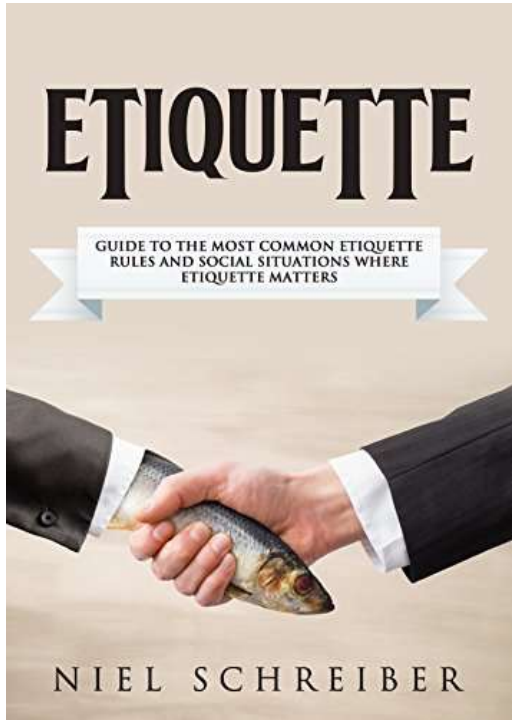
- Be fair, think at what you would like to happen to your paper
- Ask that your work is cited if it is relevant
- Do not accept the review if you do not feel qualified
- The fact that there are bad reviewers is not an excuse



Prepare your review letter

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- Start with the title

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- Start with the title
- Make a short description of the paper

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- Make a short description of the paper
- Consider the paper kind when reviewing
  Short-long, only theoretical work..

Prepare your review letter

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- Start with the title
- Make a short description of the paper
- Consider the paper kind when reviewing
  Short-long, only theoretical work..
- Assign a score to every aspects
  1. Relevance
  2. Originality
  3. Significance to the filed
  4. Technical Soundness
  5. References
  6. Presentation

Prepare your review letter

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- Typical scores can be:
  1. Bad
  2. Weak
  3. Fair
  4. Good
  5. Excellent

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- Typical scores can be:
  1. Bad
  2. Weak
  3. Fair
  4. Good
  5. Excellent

- The final conclusion that you have to draw is either
  - Accept as it is
  - Accept after minor revision
  - Accept after major revision
  - Reject

Always motivate your decision

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- A **rejection** needs a strong motivation:
  - It is already been published in another journal or conference
  - The work has no novelty (equal to previous work), give evidence
  - The work is not scientifically sound, give evidence
  - The process chosen is absolutely not adequate

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  - The work has no novelty (equal to previous work), give evidence
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  - The process chosen is absolutely not adequate
- A **major revision** needs a solid motivation:
  - Only incremental work
  - Not reproducible
  - Does not consider nor cite relevant research in the field
  - Claims are inappropriate
  - Presentation is very weak
  - Data are missing

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- A **minor revision** needs a good motivation:
  - Clarity must be improved
  - Additional results may improve the paper
  - Few references are missing
  - Some sections need rewriting
  - More details on the equipment and on the way it has been used

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- **Accept as is** needs a clear motivation:
  - Very innovative
  - Clear, concise, to the point
  - Very relevant
  - Great Impact

Write the review

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- Do not sign the review (this is debated at the moment)

Write the review

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- Do not include your final judgment, only the evaluation
  It is the editor decision in the end

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- Be formal and polite

Write the review

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  It is the editor decision in the end
- Be formal and polite
- Remember the goal is not to kill research, the goal is to be a promotor of good research

Rebuttal letter

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- Do not get emotional

Rebuttal letter

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- Do not get emotional
- Be clear and to the point
  Your rebuttal will be much stronger

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- Consider compromises (do not take them all)

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- Sometimes doing some extra work will pay more and faster than trying to get away with it

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- You do not have to please the reviewers, you have to convince the editor

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- Take a stand if needed

Example

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Dear Associate Editor,

the authors want to thank you and the reviewers for handling this manuscript and for the useful comments.

General statement on the approach chosen: (*e.g. all comments have been considered and the paper has been modified accordingly*)

Please find below a point to point response to the reviewers comment

Rev1
“the paper lacks in..”
Response
We included in the paper…

Personal Experience

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From a rejection on a very important journal but with a very very weak review..

Personal Experience

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Cumulative phase delay between second harmonic and fundamental components—A marker for ultrasound contrast agents

Libertario Demi,[a] Hessel Wijkstra,[b] and Massimo Mischi
Department of Electrical Engineering, Laboratory of Biomedical Diagnostics, Eindhoven University of Technology, Den Dolech 2, 5612 AZ, Eindhoven, the Netherlands

(Received 8 July 2014; revised 30 September 2014; accepted 3 October 2014)

Several imaging techniques aimed at detecting ultrasound contrast agents (UCAs) echo signals, while suppressing signals coming from the surrounding tissue, have been developed. These techniques are especially relevant for blood flow, perfusion, or contrast dispersion quantification. However, despite several approaches being presented, improving the understanding of the ultrasound/UCAs interaction may support further development of imaging techniques. In this paper, the physical phenomena behind the formation of harmonic components in tissue and UCAs, respectively, are addressed as a possible way to recognize the origin of the echo signals. Simulations based on a modified Rayleigh, Plesset, Noltingk, Neppiras, and Poritsky equation and transmission and backscattering measurements of ultrasound propagating through UCAs performed with a single element transducer and a submergible hydrophone, are presented. Both numerical and *in vitro* results show the occurrence of a cumulative time delay between the second harmonic and fundamental component which increases with UCA concentration and propagation path length through UCAs, and that was clearly observable at frequencies ($f_0 = 2.5$ MHz) and pressure regimes (mechanical index = 0.1) of interest for imaging. Most importantly, this delay is not observed in the absence of UCAs. In conclusion, the reported phenomenon represents a marker for UCAs with potential application for imaging.
 [http://dx.doi.org/10.1121/1.4898419]

PACS number(s): 43.25.Yw [CCC] Pages: 2968–2975

I. INTRODUCTION

Dynamic contrast-enhanced ultrasound (DCE-US) is an imaging technique where diagnostic ultrasound is used in combination with intravascular contrast agents, typically gas-filled microbubbles encapsulated in a lipid shell.[1] Examples of possible clinical applications are perfusion[2,3] and dispersion quantification.[4,5] To distinguish ultrasound contrast agents (UCAs) echo signals from tissue, the nonlinear response of UCAs to ultrasound is usually exploited. Microbubbles respond in fact to insonification resonating not just at the (fundamental) frequency of the applied ultrasound field, but also at the second harmonic frequency,[6] as well as at higher harmonics, sub-harmonic, and ultra-harmonic frequencies.[7,8] Based on these harmonic components, a variety of contrast specific imaging techniques have been developed in the past years.[9] However, tissue itself induces the formation of harmonic components as a consequence of the cumulative nonlinear distortion that occurs during ultrasound propagation through tissue,[10] de facto deteriorating the contrast to tissue ratio (CTR). Moreover, artifacts due to nonlinear propagation of ultrasound through microbubbles[11] affect common DCE-US imaging techniques, i.e., harmonic imaging, pulse inversion, and amplitude modulation, leading to possible tissue misclassification, misinterpretation of bubble concentrations, and further CTR reduction. Despite several studies and approaches being presented, e.g., exploiting the effects of insonating pressure on ultrasound phase velocity,[12] counter propagation imaging[13] and bi-spectral analysis,[14] further improvements can be achieved by improving our understanding of the interaction between ultrasound and UCAs.

Here we propose to address the different nature of the physical phenomena behind the formation of the harmonic components in tissue and UCAs, respectively, as a way to characterize the origin of the echo signals (tissue or UCAs). In tissue, harmonics are formed due to the pressure dependency of the speed of sound. In particular, when looking at the excess pressure (defined as the pressure variation with respect to the ambient pressure), the positive parts of the wave travel faster than the negative ones, resulting in a cumulative deformation (steepening) of the waveform. Consequently, the rise of new frequency components, centered at multiples of the center frequency of the undeformed pressure wave, may be observed during propagation. After experiencing such a distortion, the waveform can be thought as a linear combination of multiple pulses, each representative for either the fundamental or a harmonic component. Most importantly, the peak of the harmonic pulses anticipates in time the peak of the fundamental pulse, as effect of the waveform steepening, ultimately resulting in a negative

Personal Experience

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Cumulative phase delay between secon fundamental components—A marker fo agents

Libertario Demi,[a] Hessel Wijkstra,[b] and Massimo Mischi
Department of Electrical Engineering, Laboratory of Biomedical Diagnos of Technology, Den Dolech 2, 5612 AZ, Eindhoven, the Netherlands

(Received 8 July 2014; revised 30 September 2014; accepted 3 Oct

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Phys. Med. Biol. **60** (2015) L23–L33 — doi:10.1088/0031-9155/60/21/L23

Fast Track Communication

Cumulative phase delay imaging for contrast-enhanced ultrasound tomography

Libertario Demi[1], Ruud J G van Sloun[1], Hessel Wijkstra[1,2] and Massimo Mischi[1]

[1] Laboratory of Biomedical Diagnostics, Eindhoven University of Technology, 5612 AZ Eindhoven, The Netherlands
[2] Academic Medical Center Amsterdam, 1105 AZ Amsterdam Zuid-Oost, The Netherlands

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Received 6 August 2015, revised 7 September 2015
Accepted for publication 18 September 2015
Published 13 October 2015

Abstract

Standard dynamic-contrast enhanced ultrasound (DCE-US) imaging detects and estimates ultrasound-contrast-agent (UCA) concentration based on the amplitude of the nonlinear (harmonic) components generated during ultrasound (US) propagation through UCAs. However, harmonic components generation is not specific to UCAs, as it also occurs for US propagating through tissue. Moreover, nonlinear artifacts affect standard DCE-US imaging, causing contrast to tissue ratio reduction, and resulting in possible misclassification of tissue and misinterpretation of UCA concentration. Furthermore, no contrast-specific modality exists for DCE-US tomography; in particular speed-of-sound changes due to UCAs are well within those caused by different tissue types. Recently, a new marker for UCAs has been introduced. A cumulative phase delay (CPD) between the second harmonic and fundamental component is in fact observable for US propagating through UCAs, and is absent in tissue. In this paper, tomographic US images based on CPD are for the first time presented and compared to speed-of-sound US tomography. Results show the applicability of this marker for contrast specific US imaging, with cumulative phase delay imaging (CPDI) showing superior capabilities in detecting and localizing UCA, as compared to speed-of-sound US tomography. Cavities (filled with UCA) which were down to 1 mm in diameter were clearly detectable. Moreover, CPDI is free of the above mentioned nonlinear artifacts. These results open important possibilities to DCE-US tomography, with potential applications to breast imaging for cancer localization.

Personal Experience

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Fast Track Communication

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PHYSICS

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CORRESPONDING AUTHOR:
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Biomedical Diagnostics
Eindhoven University
Eindhoven, The Netherlands

LIBERTARIO DEMI

EDITORS' PICKS
Highlight Radiotherapy Physics Papers

What was your motivation for initiating this study?

We began this study in search of an alternative way to image ultrasound contrast agents (UCAs). In fact, several complications affect standard dynamic contrast-enhanced ultrasound (D-CEUS) imaging. This limits D-CEUS application in contexts where accurate localisation and quantification of UCA concentration are crucial, like the use of D-CEUS for detecting changes in the vasculature architecture as those due to angiogenesis: a key process in tumour growth. In particular, we wanted to verify the possibility to develop our recent discovery of a new marker for UCA into a new contrast specific imaging modality.

What is the most important finding of your study?

This study confirms the possibility to employ this new marker (the *cumulative phase delay* between the second harmonic and fundamental component of ultrasound waves) to generate contrast-specific ultrasound tomographic images. In particular, these images were free of artefacts encountered in standard D-CEUS. Furthermore, it is important to add that no contrast-specific modality exists yet for ultrasound tomography, as acoustic parameters commonly used for tomography (e.g. speed-of-sound) show changes due to the presence of UCA that are well within those caused by different tissue types. On the contrary, cumulative phase delay imaging is based on a physical phenomenon that is specific to UCA, and shows superior capabilities at detecting and localising UCA.

What are the implications of this research?

These results may find relevant application in the development of contrast-enhanced ultrasound tomography of the breast, with the aim of providing a radiation-free imaging modality that enables visualisation of the whole breast vasculature architecture in 3D. Such an imaging modality would open new horizons for the detection and localisation of breast cancer.

Personal Experience

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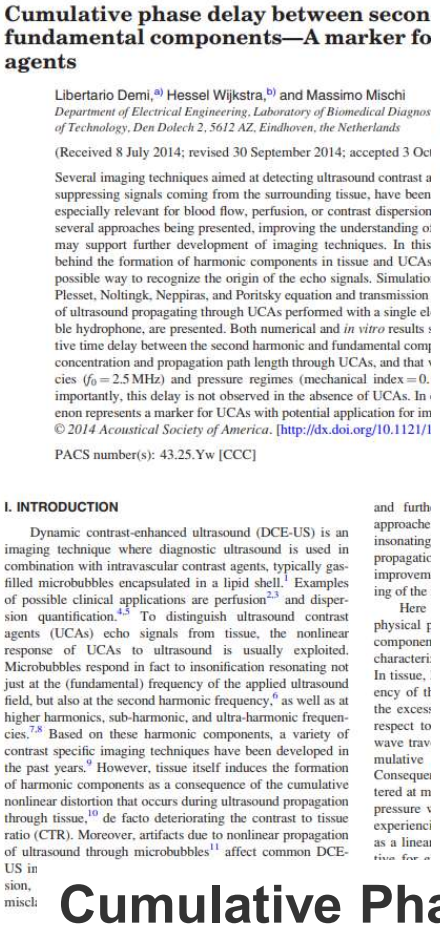

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Cumulative phase delay imaging for contrast-enhanced ultrasound tomography

Libertario Demi, Ruud J G van Sloun, Hessel Wijkstra and Massimo Mischi

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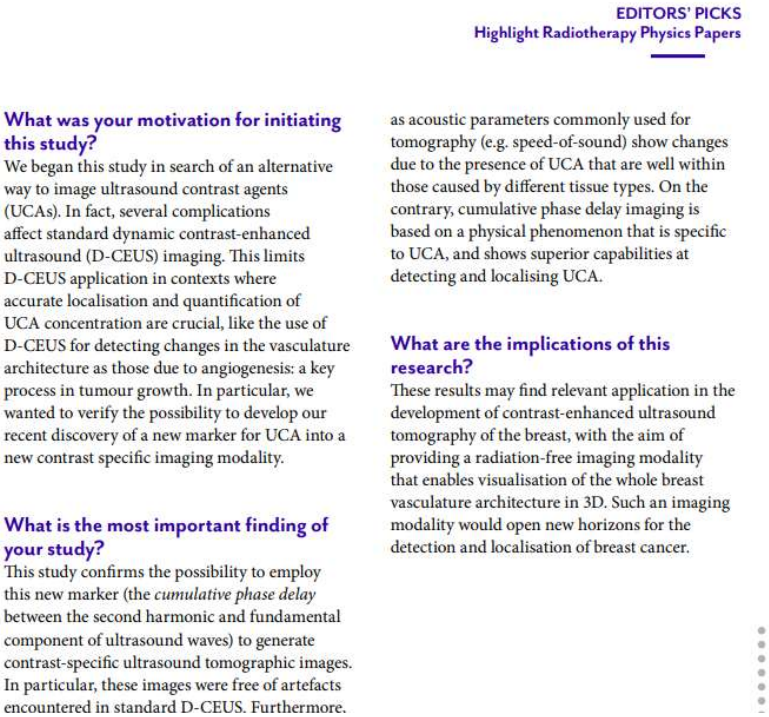

EDITORS' PICKS
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What was your motivation for initiating this study?

We began this study in search of an alternative way to image ultrasound contrast agents (UCAs). In fact, several complications affect standard dynamic contrast-enhanced ultrasound (D-CEUS) imaging. This limits D-CEUS application in contexts where accurate localisation and quantification of UCA concentration are crucial, like the use of D-CEUS for detecting changes in the vasculature architecture as those due to angiogenesis: a key process in tumour growth. In particular, we wanted to verify the possibility to develop our recent discovery of a new marker for UCA into a new contrast specific imaging modality.

What is the most important finding of your study?

This study confirms the possibility to employ this new marker (the *cumulative phase delay* between the second harmonic and fundamental component of ultrasound waves) to generate contrast-specific ultrasound tomographic images. In particular, these images were free of artefacts encountered in standard D-CEUS. Furthermore, as acoustic parameters commonly used for tomography (e.g. speed-of-sound) show changes due to the presence of UCA that are well within those caused by different tissue types. On the contrary, cumulative phase delay imaging is based on a physical phenomenon that is specific to UCA, and shows superior capabilities at detecting and localising UCA.

What are the implications of this research?

These results may find relevant application in the development of contrast-enhanced ultrasound tomography of the breast, with the aim of providing a radiation-free imaging modality that enables visualisation of the whole breast vasculature architecture in 3D. Such an imaging modality would open new horizons for the detection and localisation of breast cancer.

Cumulative Phase Delay Imaging – a new contrast enhanced imaging modality" in Proceedings on 20th European Symposium on Ultrasound Contrast Imaging, Rotterdam: Erasmus MC, 2015. Proceedings of: European Symposium on Ultrasound Contrast Imaging,, Best poster awars

Personal Experience

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Fast Track Communications

Cumulative phase delay between secon fundamental components—A marker fo agents

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Several imaging techniques aimed at detecting ultrasound contrast a suppressing signals coming from the surrounding tissue, have been especially relevant for blood flow, perfusion, or contrast dispersion several approaches being presented, improving the understanding o may support further development of imaging techniques. In this

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Fast Track Communication

Cumulative phase de contrast-enhanced ul

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Towards Dynamic Contrast Specific Ultrasound Tomography

Libertario Demi[1], Ruud J. G. Van Sloun[1], Hessel Wijkstra[1,2] & Massimo Mischi[1]

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We report on the first study demonstrating the ability of a recently-developed, contrast-enhanced, ultrasound imaging method, referred to as cumulative phase delay imaging (CPDI), to image and quantify ultrasound contrast agent (UCA) kinetics. Unlike standard ultrasound tomography, which exploits changes in speed of sound and attenuation, CPDI is based on a marker specific to UCAs, thus enabling dynamic contrast-specific ultrasound tomography (DCS-UST). For breast imaging, DCS-UST will lead to a more practical, faster, and less operator-dependent imaging procedure compared to standard echo-contrast, while preserving accurate imaging of contrast kinetics. Moreover, a linear relation between CPD values and ultrasound second-harmonic intensity was measured (coefficient of determination = 0.87). DCS-UST can find clinical applications as a diagnostic method for breast cancer localization, adding important features to multi-parametric ultrasound tomography of the breast.

Nowadays, there is growing interest in the development of imaging techniques which are capable of detecting and localizing angiogenesis and neovascularization. These processes induce specific changes in the microvascular structure, represent an established marker for tumours, and also provide indications of tumour aggressiveness[1]. In particular, dynamic contrast-enhanced ultrasound (DCE-US) imaging shows promise, with many novel approaches focusing on the direct and/or indirect characterization of the microvasculature. However, when considering the various imaging options, several challenges emerge for imaging the breast.

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