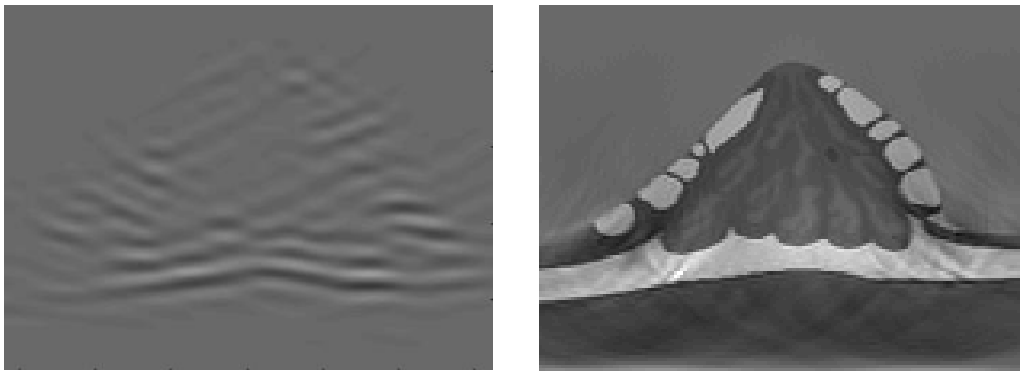
K-Space analysis for plane-wave ultrasound imaging

Georg Schmitz

Abstract: Ultrasound imaging can be considered as an inverse scattering problem in which the unknown distribution of the material parameters mass density and compressibility is reconstructed from measurements of scattered waves on the borders around the object. Unfortunately, this inverse problem is mathematically ill-posed and nonlinear: While the wave propagation is considered linear, the mapping of material parameters to measurements is nonlinear because the superposition principle is not valid: The sum of the wavefield solutions for two individual scatterers is not the correct solution when both scatterers are present because of multiple scattering.

The usual way to deal with this nonlinearity is to use the linear Born approximation neglecting multiple scattering. Based on this approximation the analysis of ultrasound imaging is possible and pulse-echo ultrasound and transmission ultrasound using plane waves will both be described in the spatial frequency domain (k-space). One result of this analysis is the fundamental half-wavelength resolution limit. Also, the characteristics of reconstruction results in transmission and reflection imaging can be explained as k-space-filtered versions of the material parameters. For reflection imaging low spatial frequencies cannot be not reconstructed, explaining the main image characteristics observed in clinical imaging, e.g. the speckle pattern and missing absolute values.

However, all limits resulting from the linear Born approximation are not necessarily valid when nonlinear reconstruction methods are applied. Simulations will be presented that demonstrate that absolute material parameter values can be reconstructed even in reflection imaging. In theory, also the half-wavelength resolution limit must not be valid. When the computational complexity and convergence issues of these methods can be overcome, ultrasound image quality would be drastically improved.



Left: Linear reconstruction (not demodulated) at 100 kHz. Right: non-linear full wavefield inversion of a numerical breast phantom using 100 kHz – 200 kHz ultrasound.

Session: Ultrasound Velocity Imaging and Diagnostics

Fast imaging and vector flow estimation, an engineer's perspective.

Svetoslav Nikolov

Abstract: Algorithms to estimate the 2D and even 3D vector flow were introduced in the 1990s. Almost 20 years later, only few systems have
vector flow imaging (VFI) implemented, and VFI is still used in primarily in research. Fast imaging, producing several hundreds, even thousand of frames per second, was also introduced in the 1990s. There are, though, few commercial systems with fast imaging acquisition.

Why is the ultrasound industry so slow to adopt such breakthrough technologies? For a technology to be accepted, it must make a difference in clinical outcome at an affordable price. The combination of fast imaging and vector flow is promising, in that it gives the possibility to capture fine details in the hemodynamics, such as turbulence and back flow in carotid, and to estimate both fast and slow flow with high precision. It allows to derive new quantitative measures such as wall shear stress, pressure change, and to calculate volume flow with higher precision.
In this presentation we will look into algorithms for flow estimation and fast imaging. We will also discuss the challenges in the system architecture and implementation.

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Contrast enhanced high frame rate ultrasound, towards diagnostic application

Erik Groot Jebbink

Abstract: Endovascular treatment of stenotic and aneurysmatic lesions is the preferred choice of treatment nowadays. However, in some cases reintervention is indicated because of restenosis due to progression of atherosclerotic plaque or thrombotic events. Local blood flow perturbations seem to play a crucial role in this setting. Full quantification of blood flow is not trivial, up till now high frame rate contrast enhanced ultrasound imaging seems to be a promising modality. Currently we are preparing a study to investigate the diagnostic value of this technique.

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Imaging the velocity and dispersion of ultrasound-contrast-agents for prostate cancer localization.

Ruud van Sloun

Abstract: Prostate cancer is the most frequently diagnosed cancer in men aside from skin cancer. Angiogenesis is known to play a central role in the growth of tumours towards a metastatic or a lethal phenotype. To reveal those changes in the vascular architecture that are associated with angiogenesis, we have recently introduced several advanced contrast-enhanced ultrasound technologies that aim at quantifying the notoriously chaotic nature of tumour vasculature: We assess contrast-agent kinetics through the estimation of their flow velocity and dispersion in the vascular net, quantify the heterogeneity of blood vector velocity patterns, and determine the density and tortuosity of traced flow trajectories. These new CEUS techniques show great promise for the detection of prostate cancer.

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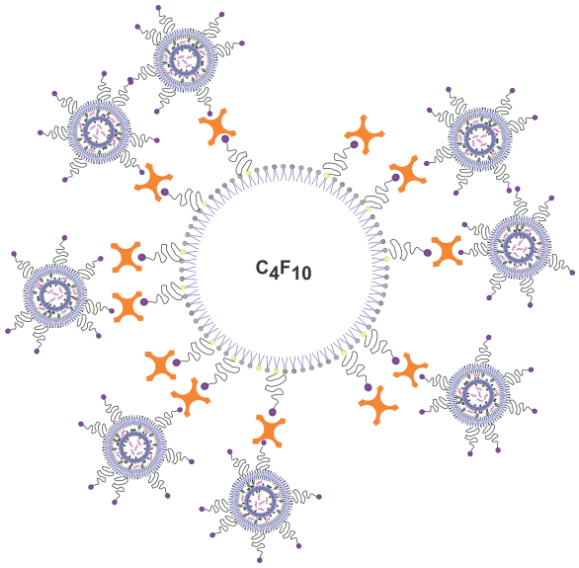
Session: Ultrastound Contrast Imaging and Therapy

Drug loaded microbubbles for ultrasound triggered drug delivery

Ine Lentacker

Abstract: The last decade it has become clear that ultrasound contrast agents (“microbubbles”) are very promising drug delivery agents as they facilitate drug release and uptake in ultrasound treated areas. We developed the concept of “nanoparticle loaded microbubbles” in which drugs are pre-complexed into nanoparticles and subsequently loaded onto the microbubble shell. This allows to follow drugs loaded nanoparticles with contrast enhanced ultrasound imaging and promote their release and uptake selectively in ultrasound treated areas using more intense ultrasound pulses. As such, this concept can lead to lower drug doses and fewer side effects. This presentation will focus on the concept of drug-loaded microbubbles and how this concept could be particularly useful for ultrasound guided cancer immunotherapy, thereby circumventing the current expensive and complex *ex vivo* procedures.



Nanoparticle-loaded microbubble I Drugs are loaded into lipid nanoparticles and coupled onto the microbubble surface of lipid-shelled microbubbles.

References

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2. Dewitte et al. Theranostic mRNA-loaded Microbubbles in the Lymphatics of Dogs: Implications for Drug Delivery. **Theranostics 2015**. 5(1):97-109.
3. De Cock et al. Sonoprinting and the importance of microbubble loading for the ultrasound mediated cellular delivery of nanoparticles. **Biomaterials 2016**. 83, 294-307.

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Mechanisms for single-cell drug delivery with microbubbles

Guillaume Lajoinie

Abstract: Ultrasound-driven microbubbles are attractive for a variety of applications in medicine, including real-time organ perfusion imaging and targeted molecular imaging. In ultrasound-mediated drug delivery, bubbles decorated with a functional payload become convenient transport vehicles and offer highly localized release. How to efficiently release and transport these nanomedicines to the target site remains unclear owing to the microscopic length scales and nanoseconds timescales of the process. Here, based on side view ultra high-speed imaging and side-view fluorescence imaging, we discuss the role of non-spherical bubble oscillations in releasing the bubble payload, and in generating microstreaming to transport it. Measured transport distance and intrinsic bubble behavior are in good agreement with the modeled predictions. This new physical insight allows for optimizing the therapeutic use of targeted microbubbles for precision medicine.

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High-Precision Acoustic Measurements of the Nonlinear Dilatational Elasticity of Phospholipid-Coated Monodisperse Microbubbles

Tim Segers

Abstract: The acoustic response of phospholipid coated ultrasound contrast agents (UCA) is dramatically affected by the stabilizing shell around the microbubbles. The elasticity of the microbubble shell increases the resonance frequency, and its nonlinear behavior promotes the generation of harmonic echoes that are currently exploited for contrast-enhanced ultrasound imaging. The harmonic scattering of contrast bub- bles has been quite successfully modelled by the rather ad-hoc assumptions in the model of Marmottant et al., where the nonlinear behaviour was captured in a linear elastic part around equilibrium, a rup- tured part for bubble expansion and a buckling part upon bubble compression. Here we present for the first time high-precision experimental data of acoustic measurements of the exact non-linear behavior of these bubbles. Microbubble viscoelastic shell properties were measured as a function of the ambient pressure-controlled surface dilatation (pressures ranging from 70 to 140 kPa) through acoustic attenua- tion spectra of monodisperse bubble suspensions formed by flow-focusing. The bubble samples had mean radii ranging from 1.5 to 3.3 μm, with a typical PDI of 5%, and the bubbles were coated by DPPC and DPPE-PEG5000 mixed at PEG molar fractions of 5.0, 7.5, and 10.0%. Bubble size as a function of am- bient pressure was measured optically. The obtained dilatational elasticity was found to be independent of the absolute microbubble size and PEG molar fraction. However, in contrast to the constant elasticity in the Marmottant model for elastic oscillations, shell elasticity was found to be highly dependent on the surface dilation. The dilatational elasticity curve was integrated with respect to bubble area to find the dilatational interfacial tension of phospholipid-coated microbubbles. For compressed bubbles, it increases during decompression, first rapidly, and then more slowly from zero to the surface tension of the surrounding aqueous medium. This new insight will allow for more accurate modeling of nonlinear bubble dynamics.

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Improving (nano-) drug delivery using ultrasound and microbubbles

Twan Lammers

Abstract: The combination of ultrasound and microbubbles in increasingly employed to improve drug delivery to pathological sites. In the last 5-10 years, our group and others have developed microbubble materials and ultrasound methodologies to enable more efficient transport of pharmacologically active agents to and into tumors, and across the blood-brain barrier. Several of these strategies have recently been translated to the clinic, and the initial evidence obtained in patients suggests that

ultrasound (in particular when combined with microbubbles) holds significant potential for more efficient disease treatment.

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Session: Ultrasound Breast Imaging and Robotics

The role of breast ultrasound

Jeroen Veltman

Abstract: Clinical ultrasound of the breast has been a part of breast diagnostics for over 60 years. Ultrasound is a usefull tool because it can tell the difference between fluid-filled cysts (benign) and solid masses (could be cancer). Ultrasound can also be used as an accurate tool for biopsy. For the primary detection of lesions ultrasound is usually not used.

In clinical practice breast ultrasound is mainly used as an additional tool to clarify a palpable lesion, mammographic density or MRI finding. Unfortunately, hand-held breast ultrasound is not perfect in finding all lesions and not perfect in differentiating between benign and malignant lesions.

Improving the performance of breast ultrasound by training the radiologist is helpful. Technical improvements in ultrasound diagnostics also contribute to improving the detection and classification of breast lesions. 3D whole breast ultrasound, computer assisted diagnosis and even robot assisted whole breast ultrasound can help in finding and characterizing the lesions based on their ultrasound characteristics or prior knowledge. Tissue characteristics that can be found with ultrasound with additional tools like elastography and opto-acoustic imaging can help in classifying lesions as probably benign.

In this presentation I will discuss the role of and new developments in breast ultrasound.

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Laser-Induced ultrasound in multimodal acoustic breast imaging

David Thompson

Abstact: For the last decade the Biomedical Photonic Imaging group at the University of Twente has been one of the pioneers in the field of photoacoustic breast imaging. The recently launched H2020 PAMMOTH project will combine this expertise with ultrasound reflection tomography and speed-of-sound imaging. This combination will overlay the functional information from photoacoustic imaging with the anatomical information from ultrasound reflectivity. The speed-of-sound imaging will support the

accurate reconstruction of images based on actual tissue properties. The ultrasound transmission will be achieved using the non-conventional means of laser-induced ultrasound (LIUS). In this talk we will

present the background and expected advantages of the method. We will report on the ongoing development of LIUS transmitters and imaging experiments and conclude with future plans.

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3-D automated breast elastography for improved breast cancer detection

Gijs Hendriks

Abstract: The automated breast volume scanner (ABVS) is an operator-independent 3-D ultrasound system for breast cancer detection. Although ABVS imaging has a high sensitivity, specificity remains a limitation resulting in unnecessary biopsies. Compared to benign lesions, malignant lesions are often stiffer, and grown into surrounding tissue resulting in reduced strains inside the lesion and shear strains around it. Mapping of (shear) strains might be an excellent choice to improve discrimination between benign and malignant lesions. In this study, we implemented ultrasound elastography in an ABVS and showed that it was possible to map (shear) strains for quantification of lesion stiffness and bonding.

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About what Robotics has to offer for Oncology

Stefano Stramagioli

Abstract: The presentation will address a couple of methods and devices which involve robotics technology couple to imaging in order to target lesions in oncology. The problems and approaches will be described and discussed.

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