Karolinska Institutet

Institutionen för klinisk vetenskap, intervention och teknik (CLINTEC), Enheten för medicinsk bild, funktion och teknologi

Contrast Enhanced Ultrasound (CEUS) in Breast Tumors

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ABSTRACT

Contrast-enhanced ultrasound or CEUS is a combination of the pharmacokinetics of contrast agents (or microbubbles-based ultrasound contrast agents), the signal processing of these agents and the contrast-specific imaging modality.

One of the main objectives of this method is to gather vascular information (from large vessels to capillaries) in different organs or tumors by increasing the signal intensity from blood.

The **aim** of this thesis is to evaluate the kinetic value of real time harmonic imaging contrast-enhanced ultrasound (CEUS) in breast tumors as a differential diagnostic tool and correlate it with prognostic factors in invasive breast carcinomas (Studies II and IV).

Successful introduction of a new imaging method always requires studies evaluating the technical parameters for optimal diagnostic performance. Concerning CEUS for imaging breast tumors, the mode of injection and dose of injected agent can be identified among these parameters. Therefore two methodology studies are included in this work (Studies I and III).

In **Study I** we evaluated which method is to prefer between bolus and continuous infusion of equal doses of contrast agent, in order to achieve the best technique to gather vascular information of breast tumors. We observed that the qualitative assessment of the curves after bolus administration of contrast agent provided sharply demarcated tumors with clear visible wash-in and wash-out patterns in all cases. The continuous infusion with the same doses of contrast agent was not able to show a clear wash-in/wash out in any case.

In **Study II** we investigated whether kinetic parameters of real time harmonic CEUS imaging could be used to differentiate between benign and malignant breast tumors. The study showed that real time harmonic contrast enhanced ultrasound as a kinetic tool in the breast can detect significant differences between benign and malignant tumors, when evaluating two main parameters: time-to-peak and washout ratio. Both parameters have been observed to be earlier/faster in malignancies when compared with benign tumors. We observed the fact that after 21 seconds the malignant tumors tends to eliminate more than 50% of the total amount of contrast, while the benign tumors tends to eliminates less than 50 % (mean values are 69% respective 36% elimination of contrast at 21 seconds).

In **Study III** we compared different doses of injected contrast agent in order to establish an optimal dose for the diagnosis of invasive breast cancer using real time harmonic CEUS. The results were, in terms of diagnostic features, that the optimal way to evaluate kinetic features of invasive breast tumors using real time contrast-enhanced ultrasound harmonic imaging was with a bolus injection of contrast agent of either 2.4 mL or 4.8 mL.

In **Study IV** we correlated real time harmonic CEUS kinetic parameters with traditional and molecular prognostic factors in invasive breast cancer. The results were that invasive breast carcinomas exhibiting earlier peak enhancement and fast elimination of microbubbles contrast agent at contrast-enhanced ultrasound are associated with established predictors of poor prognosis.

In **conclusion** this thesis demonstrates that kinetic parameters of real time harmonic CEUS with a bolus injection of either 2.4 or 4.8 mL contrast agent has potential for diagnosis, differential diagnosis and prognosis of invasive breast cancer tumors.

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