EFSUMB Journal Club – Issue 2

The EFSUMB Journal Club regularly reviews the leading Ultrasound-related journals, sharing with EFSUMB members selected relevant publications, providing values and critiques of the work.

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EFSUMB Technical Review – Update 2023: Contrast-Enhanced Ultrasound (DCE-US) for the Quantification of Tumor Perfusion

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Purpose DCE-US (Dynamic contrast-enhanced ultrasound) is a method for quantifying the intensity of enhancement in CEUS. Subjective impressions regarding enhancement can be objectified through quantification. The current work is based on a first EFSUMB proposal from 2012 (*Dietrich CF, Averkiou MA, Correas JM et al. An EFSUMB introduction into Dynamic Contrast-Enhanced Ultrasound (DCE-US) for quantification of tumour perfusion. Ultraschall in der Medizin 2012; 33: 344–351. doi:10.1055/s-0032–1313026*). In addition to the basics of DCE-US, clinical studies on DCE-US are included. Important clinical indications are the anti-inflammatory therapy monitoring of chronic inflammatory bowel diseases, the differential diagnosis of liver tumors and the therapy response of tumors. The monitoring of response of tumors to antiangiogenetic therapy is not assessed solely on the basis of changes in tumour size (RECIST). The response to therapy is also assessed by changes in tumor perfusion (mRECIST). DCE-US can be an important method to assess the effect of antiangiogenetic therapies.

Material and Methods The technical requirements, implementation and meaning of the parameters are described. DCE-US is performed with pure blood pool agents, such as (SonoVue/Lumason [sulfur hexafluoride with a phospholipid shell, Bracco spa], or Definity [Octafluoropropane with a phospholipid shell, Lantheus Medical Imaging, Billerica MA, USA]. The contrast agent (UCA) is applied either by an intravenous bolus injection or an infusion of UCA. The bolus technique quantifies the entire course of contrast kinetics, from wash-in to washout and is preferred for the assessment of tumor perfusion. After a bolus injection of UCA, the wash-in/wash-out analysis (bolus transit) is performed. This is analyzed by imaging in one plane at a low mechanical index (MI) at approximately 10 frames per second for the duration of the enhancement.

The average CEUS signal intensity within a region of interest (ROI) is calculated in linear units and plotted as a function of time. This is a time-intensity curve (TIC). It shows the phases of progressive increase

in the enhancement of the contrast agent in the ROI (wash-in phase) and the subsequent phase of slow decrease in contrast signal intensity (wash-out phase). A distinction is made between time-related parameters and signal intensity-related parameters. Time-to-peak (TP), rise time (RT), mean transit time (MTT), peak intensity (PI) and area under the curve (AUC) are proposed as primary parameters. All others are derived from these parameters.

The signal intensity in DCE-US is proportional to the number of microbubbles. From this it is deduced that the TIC parameters represent the perfusion of the corresponding region.

Some signal-related parameters (peak intensity, area under the curve) correlate more strongly with the local blood volume of the region, while other time-related parameters (TTP, WIT, AUC) tend to reflect the blood flow. The total AUC (the area under the curve) is divided into two components: the AUC in the wash-in phase up to the peak intensity PI (WIAUC) and in the wash-out phase from the peak intensity to the predefined end time (WOAUC). The total AUC is the sum of WIAUC + WOAUC.

The infusion technique is followed by a disruption-replenishment technique. Refilling kinetics describe the replenishment of microbubbles during the infusion of UCA. The disruption replenishment method is carried out at a steady-state high signal enhancement level.

Results The paper discusses the selection of DCE-US parameters, DCE-US study design, study time points and other technical and methodological aspects. An important question is which DCE-US technique and which parameter should be used and evaluated in the different clinical situations. In oncology, monitoring or even predicting treatment success are important indications for the use of DCE-US. The parameters that enable early assessment or prediction of treatment success or failure are of clinical importance. Theoretically, changes in vascular dynamics (blood flow) may occur before a change in blood volume is visible. However, this has not yet been clearly demonstrated with DCE-US. One parameter that could be used in bevacizumab therapy of metastases is the mean transit time (MTT). However, there are still no clear and definitive data and recommendations. It is still unclear at which clinical therapy points DCE-US should be used. As a rule, imaging is performed before therapy and as part of follow-up examinations. Early time points for follow-up have sometimes been added, in particular a DCE-US examination after the first cycle of chemotherapy.

Conclusion Modern oncological therapies are not only aimed at reducing the size of the tumor. A tumor can still have a high but relatively normal blood volume or normal blood flow. Therefore, more sophisticated DCE-US parameters than those related to blood volume or perfusion may be needed to describe DCE-US patterns that correlate with vascular architecture. There are models that allow to derive such additional information. However, they are not used in clinical practice. Finally, the described DCE-US parameters provide a temporal analysis of DCE-US examinations, not a spatial analysis. The analysis of vascular architecture, however, also requires a spatial component. The placement of more than one ROI in a tumor, e. g. in the periphery and in the center, is the simplest approach to add a spatial analysis.

Strength The article shows that DCE-US can be promising in oncology, particularly in the assessment of response to targeted antiangiogenic therapies. This article provides general information on the technique and parameters used in DCE-US quantification and recommendations on how to apply them in order to a standardized approach that can improve clinical management.

Weaknesses In order to incorporate DCE-US into the workflow, it would be helpful to evaluate in future studies the parameters whose dynamics demonstrate the response to antiangiogenic therapy and justify a continuation or change in the therapeutic regimen.

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Tips and tricks in ultrasound-guided musculoskeletal interventional procedures

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The article includes Ultrasound visualisation and highlights accurate guidance for a variety of percutaneous, minimally invasive procedures in the musculoskeletal system including joint (intra-articular) injections or aspirations, intra-bursal injections, peritendinous, and perineural injections. Ultrasound is a safe, portable, and widespread modality that can be used to assist the proceduralist in localising the needle tip in such cases, to ensure safe and accurate delivery of the medication, most frequently a solution of steroid and anaesthetic. This review aims to provide a foundational approach to ultrasound-guided procedures in the musculoskeletal system, offering tips and tricks that can be employed in many different procedures including intra-articular, juxta-articular, and perineural injections for a multitude of clinical scenarios. Technical considerations regarding ultrasound transducer selection, sonographic technique, as well as common indications, contraindications, and complications of these procedures, are presented. Additionally, a variety of pharmacologic considerations for proceduralists contemplating ultrasound-guided injections are discussed.

Strength:

- Pictorial display of methods in various applications
- Systematic overview of various approaches and their technical tips and tricks
- Explained pharmacologic considerations and effects of various injections on the tissue and their appearance on Ultrasound
- Practical useful information

Weaknesses:

- Insufficiently detailed information
- Only general principles of US guided interventional procedures are described without detailed methodology for various anatomical locations.

Personal opinion:

- The Authors report a review about a variety of percutaneous procedures in musculoskeletal applications that are traditionally performed blindly but may be more easily or more accurately performed with the real-time assistance of ultrasound guidance. This article is useful as a short guide and selection of the procedures for beginners and also advanced users and MSK Ultrasound specialists.