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Quantitative contrast enhanced ultrasound of the liver for time intensity curves—Reliability and potential sources of errors

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ABSTRACT

Introduction: Time intensity curves for real-time contrast enhanced low MI ultrasound is a promising technique since it adds objective data to the more subjective conventional contrast enhanced technique. Current developments showed that the amount of uptake in modern targeted therapy strategies correlates with therapy response. Nevertheless no basic research has been done concerning the reliability and validity of the method.
Patients and methods: Videos sequences of 31 consecutive patients for at least 60 s were recorded. Parameters analysed: area under the curve, maximum intensity, mean transit time, perfusion index, time to peak, rise time. The influence of depth, lateral shift as well as size and shape of the region of interest was analysed.
Results: The parameters time to peak and rise time showed a good stability in different depths. Overall there was a variation >50% for all other parameters. Mean transit time, time to peak and rise time were stable from 3 to 10 cm depths, whereas all other parameters showed only satisfying results at 4–6 cm. Time to peak and rise time were stable as well against lateral shifting whereas all other parameters had again variations over 50%. Size and shape of the region of interest did not influence the results.
Discussion: (1) It is important to compare regions of interest, e.g. in a tumour vs. representative parenchyma in the same depths. (2) Time intensity curves should not be analysed in a depth of less than 4 cm. (3) The parameters area under the curve, perfusion index and maximum intensity should not be analysed in a depth more than 6 cm. (4) Size and shape of a region of interest in liver parenchyma do not affect time intensity curves.

1. Introduction

Due to recent advances in angiogenesis and its use for therapeutic indications [1], e.g. tyrosine kinase inhibitory therapy in gastrointestinal stromal tumours it is obvious that for these purposes new imaging modalities are needed. The commonly used Response Evaluation Criteria in Solid Tumors (RECIST) [2] criteria based on the diameter of lesions do not fulfil the requirements for functional assessment of tumour response to the targeted therapies mentioned [3,4].

The use of wash-in and wash-out curves of contrast agents are proposed as a more functional and distinct analysis of this issue. Hereby the change of brightness over time after injection of a contrast agent monitors the inflow and outflow of a contrast agent representing the vitality of a tumour. So in a second step the changes of the vascularisation can be interpreted as a response to a certain therapy [5].

Recently contrast enhanced ultrasound with ultrasound contrast agents has gained acceptance especially in the characterisation and detection of liver tumours [6,7]. Ultrasound contrast agents of second generation stay mainly in the vascular bed and therefore represent real vascularisation in comparison to conventional contrast agents used in contrast enhanced computed tomography and contrast enhanced magnetic resonance imaging [8]. Contrast enhanced ultrasound reveals real-time imaging as well as an excellent spatial resolution and allows a nearly complete separation between tissue signal and contrast signal using current sophisticated contrast subtraction methods. Therefore con-

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trast enhanced ultrasound is especially suitable for time intensity curves.

Despite many studies published in the literature up to now there is no consensus concerning

- the validity of the parameters used.
- the different principles transforming the raw ultrasound signals into the resulting curve to be analysed (raw data—smoothing).
- the comparability of different software sources used. Mainly the latter are offered by the manufacturer of the ultrasound machine only.

In this study the stability of certain parameters against horizontal and depth changes as well as for the different size and shapes of regions of interest were analysed.

2. Patients and methods

2.1. Patients

31 consecutive patients were examined for the detection and characterisation of liver tumours or diffuse liver disease. All patients gave oral informed consent to participate in that study.

2.2. Methods

Video sequences in digital format for at least 60 s each were recorded and analysed with a prototype software system for the assessment of time intensity curves, at this time commercially not available. Loops with representative liver tissue were investigated.

Table 1
Parameters calculated from the time intensity curve and their explanation.

Parameter		Explanation
Area under the curve	AUC	Calculated integral for the time intensity curve
Maximum intensity value	IMAX	Highest value of the curve
Mean transit time	MTT	Time from the rising of the intensity up to decrease to 50% of maximum intensity
Perfusion index	PI	Area under the curve divided through mean transit time
Rise time	RT	Time from 10% to 90% of maximum intensity
Time to peak	TTP	Time from time point zero to maximum intensity

The following parameters were investigated: area under the curve (AUC), maximum intensity (IMAX), mean transit time (MTT), perfusion index (PI), time to peak (TTP), rise time from 10% to 90% of IMAX (RT) (Table 1) [9–14]. The influence of depth (different tumour positions), lateral positioning (analysis of a lesion compared to representative liver parenchyma) as well as shape and size of the region of interest (region of interest, larger and smaller tumours) were analysed to examine the reliability of the method. Tissue gain control was set manually in precontrast modus.

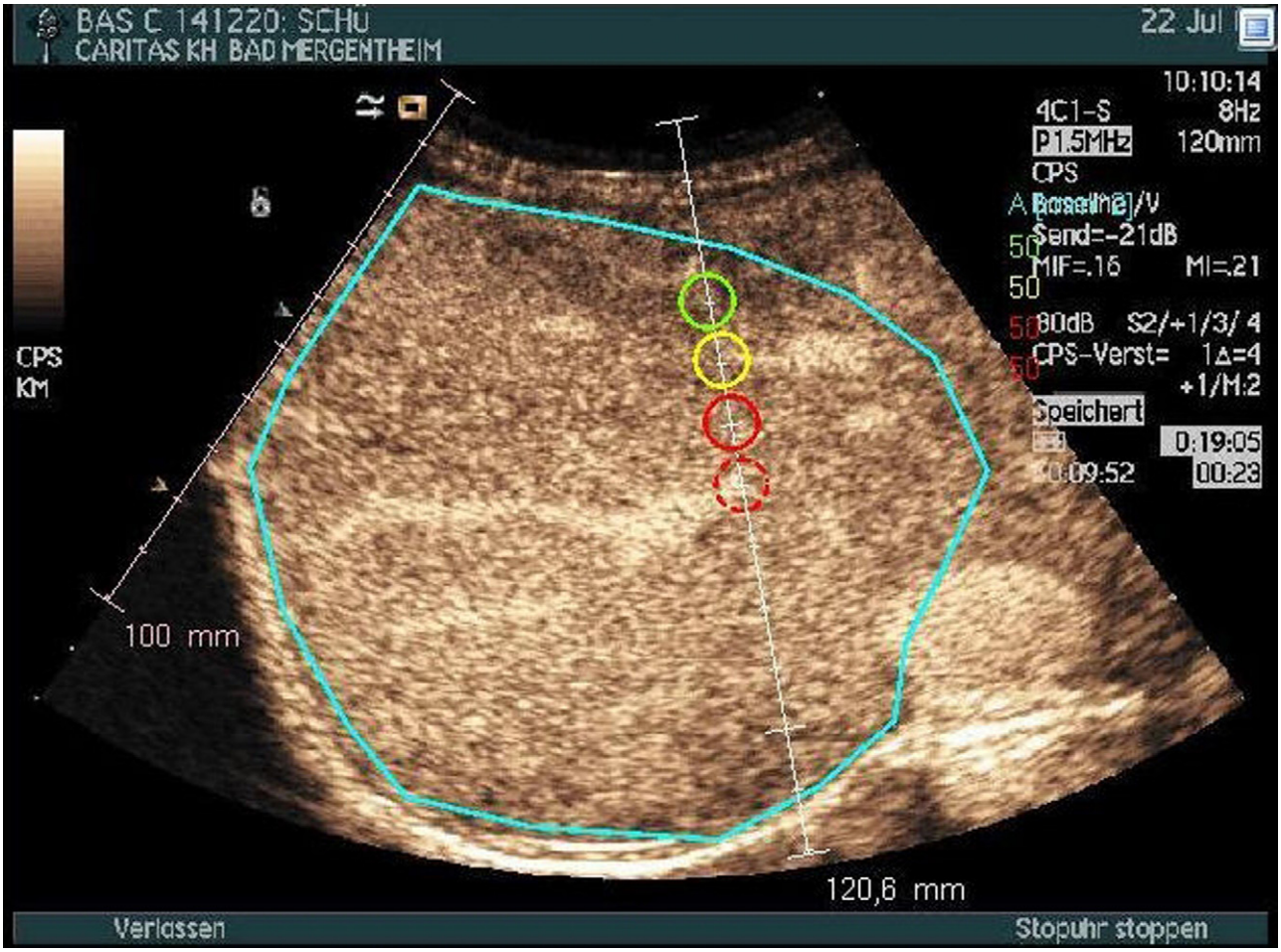

Fig. 1. Time intensity curve parameters: in normal liver tissue parameters were analysed concerning their variation in different depths.