Perfusion CT and US of colorectal liver metastases: a correlative study of two dynamic imaging modalities

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Abstract

The purpose of this study was to evaluate the correlation between dynamic-contrast-enhanced computed tomography (DCE-CT) and first-pass dynamic-contrast-enhanced ultrasound (DCE-US) of normal appearing liver parenchyma and of colorectal cancer liver metastases. Thirty patients with colorectal liver metastases underwent DCE-CT and US. To obtain DCE-US reproducibility measurements double contrast-passages (2x2.4ml Sonovue i.v.) were acquired. From several DCE-US-derived perfusion indices, the slope-value scored best with a reproducibility concordance correlation coefficient ranging from 0.75–0.93 and overall highest correlation to DCE-CT-derived variables (r=0.52–0.73). The DCE-US-based tumour-to-liver perfusion gradient also showed a low test-retest variability and moderately correlated to DCE-CT (concordance correlation coefficient 0.87–0.92; r =0.57–0.59). To conclude DCE-US-based slope-value and tumour-to-liver perfusion gradient correlate best with DCE-CT perfusion values. However, both techniques cannot be used interchangeably. DCE-US should be restricted for studies in which a considerable change in perfusion is expected and for patients with a relatively high tumour blood-flow at baseline.
Introduction

The efficacy of systemic chemotherapy of colorectal cancer liver metastases (CRLM) has improved with the recent incorporation of novel compounds, which include angiogenesis inhibitors directly aimed at reducing tumour perfusion. Adequate and early evaluation of response to these treatments remains difficult, since the generally used response evaluation criteria in solid tumours (RECIST) are based upon reduction in size. Several dynamic imaging modalities and mathematical models have been proposed to quantify changes in liver tissue perfusion at an early time-point after the start of treatment. Whether these modalities can be used interchangeably is unknown.

Dynamic contrast-enhanced CT (DCE-CT) imaging techniques use freely diffusible iodine-based contrast agents to generate a linear relationship between contrast concentration and image density in Hounsfield Units. Thus far, a limited number of studies using DCE-CT all demonstrated the feasibility of the DCE-CT technique to monitor changes in perfusion induced by anti-angiogenic compounds.

Dynamic contrast-enhanced ultrasound (DCE-US) is an inexpensive and widely available technique. The introduction of US contrast microbubbles has improved the ability to image angiogenesis and to monitor response to treatment. The phospholipid-based microbubbles encapsulate an inert gas, which will generate non-linear resonances when exposed to a US pulse allowing an enhanced view of the vascular network. Semi-quantitative perfusion measurements can be derived from the time-intensity-curve. The measured values strictly refer to the intravascular compartment and are not confounded by extra-vascular diffusion (blood pool agent).

One major problem concerning quantification of perfusion indices derived by this technique is that adequate reference feeding vessels are most often lacking within the examined range. There is need for validation of DCE-US derived variables before the technique can be implemented as surrogate marker for response to anti-tumour therapy.

The main purpose of this study was to evaluate whether a correlation would be present between maximum-slope method DCE-CT and first-pass time-concentration curve DCE-US of normal appearing liver parenchyma and of CRLM. Secondary aims were the determination of which DCE-US-derived perfusion parameter correlated best with DCE-CT-derived perfusion values and the assessment of novel parameters for which visible feeding vessels for reference are not required.
Materials and methods

Patient Selection:
Between January 2007 and June 2008, 30 consecutive patients (17 male, 13 female) of a mean age of 61 (range 35 - 75) with histologically confirmed CRLM, suitable for either surgical resection and/or radiofrequency ablation, were included. In 18 patients the CRLM were present at the time of diagnosis of the primary tumour (synchronous); in 12 patients the metastases had developed in the follow-up period (metachronous). Fourteen patients had received chemotherapy prior to this study. The mean size of the CRLM was 40 mm (range 11 – 70 mm). All patients underwent both a DCE-CT scan of the upper abdomen and a DCE-US of the liver at least 4 hours apart to avoid possible interference between the two contrast media. Exclusion criteria were a history of adverse reactions for either iodine-based contrast agents or sulphur hexafluoride-filled microbubbles, renal impairment (glomerular filtration rate <45 ml/min) and known coronary artery disease, myocardial infarction, unstable angina, acute cardiac failure, severe rhythm disorders, acute endocarditis or prosthetic valves. All examinations were performed within a maximum of 24 h prior to surgery. In all patients the treatment plan was with curative intent; the radiological information from both the CT and US studies were used to determine the definitive treatment strategy. The study was approved by the institutional ethical committee and all patients gave written informed consent. The procedures carried out in patients were in accordance with the ethical standards of the world medical association (Declaration of Helsinki).

DCE-CT protocol
Dynamic CT perfusion measurements were obtained on a 64-slice multi-detector CT scanner (Somatom Sensation; Siemens, Erlangen, Germany). A 12-phase helical CT scan of the total liver volume (collimation 0.6 mm; rotation time 0.33 sec; pitch 0.75) was acquired before and 11 times after rapid injection (6 ml/s) of 100 ml low-osmolar non-ionic contrast agent with an iodine concentration of 300 mg/ml (Ultravist-300 Iopromide; Schering A.G., Berlin, Germany) and 20 ml saline chasing bolus into the left antecubital vein, using an injection pump through an 18 g needle. To start the post-contrast scans, bolus tracking (threshold 100 HU) was used by placing a region of interest (ROI) in the right atrium. With a minimal interscan delay of 3-4 sec in between two series, the first four series were obtained in one single breath-hold at maximum inspiration. After the first series one breath out and breath in command (lasting 8 sec) was given before adding the second two series in one single breath-hold at maximum inspiration. This was repeated until a total of 11 series were acquired. The 10th series (considered as the portal venous phase series) consisted of a single breath-hold scan in which the entire (upper and lower) abdomen was scanned at conventional tube
voltage and current (120 kV and maximum 180 mAs with dose modulation). In all other series a fixed lower tube current was used to reduce radiation exposure (120 kV and 80 mAs). The last and 12th series was performed at equilibrium after approximately 300 sec. All series were reconstructed in both 5 mm contiguous axial slices and thin overlapping axial slices (slice width 1.5 mm; reconstruction increment 1.0 mm) for optimal visualization in the multiplanar reconstruction mode of the 3D fusion program. The entire protocol has previously been described in more detail. The effective dose, expressed according to the International Commission on Radiological Protection recommendations, measured with commercially available software (CT-Expo; G. Stamm, Medizinische Hochschule, Hanover, Germany using Monte Carlo simulations of anthropomorphic phantoms) was approximately 24.0 mSv (11x1.5 mSv + 1x7.5 mSv) for the dynamic CT perfusion protocol. For a conventional dose 4-phase CT this would be approximately 20.7 mSv (3x4.4 mSv + 1x7.5 mSv). Image fusion was performed with a commercially available 3-D image fusion program (Vinci 2.36.0, Max-Planck Institute for Neurological Research, Cologne, Germany). The 12 series were fused by a combination of automated and manual image shifting using coloured transparent image overlay methods. The 10th and portal venous phase series was chosen as reference to which all other series were registered in 5 mm contiguous axial slices. For quantification of tissue perfusion in normal appearing liver parenchyma and in CRLM, ROIs (including as many tumour lesions as visible, excluding large visible vessels traversing tumour tissue) were manually drawn using the software program Basama Perfusion 3.0.7.1 (Kanazawa, Ishikawa, Japan). This program was also used for the creation of blood flow maps. Tissue perfusion or blood flow (BF tissue) in ml/min/100g was estimated as the maximum slope (Slope tissue) of the tissue time-density curve in Hounsfield Units (HU) per second divided by the peak arterial enhancement (Ampl feeding vessel (HU)) in HU (Eq. 1):

\[ BF_{tissue} (\text{ml/min/100g}) = \frac{\text{Slope}_{tissue} (\text{HU/sec})}{\text{Ampl}_{\text{feeding vessel}} (\text{HU})} \]  

Eq. 1

The mathematical technique has been fully described. Due to the dual blood supply of the liver, hepatic tissue perfusion was divided into hepatic artery and portal venous perfusion as the maximum slope of the tumour time-density curve before versus after the splenic peak enhancement divided by, respectively, the peak aortic and portal enhancement (Fig. 1). Upon dividing the perfusion value of the tumour tissue (BF tumor) by the perfusion value of the normal appearing liver parenchyma (BF liv) we introduce a novel parameter, which we refer to as the perfusion gradient G. Since in equation 1 the peak enhancement for the reference feeding vessel is similar in BF tumor and BF liv, no maximum amplitude of contrast enhancement from a reference vessel (A) is needed.
\[
\frac{G_{\text{tum/liv}}}{\text{BF}_{\text{tum}}/\text{BF}_{\text{lv}}} = \frac{(\text{Slope}_{\text{tum}}/\text{Ampl}_{\text{vessel}})}{(\text{Slope}_{\text{lv}}/\text{Ampl}_{\text{vessel}})} = \frac{\text{Slope}_{\text{tum}}}{\text{Slope}_{\text{lv}}}
\]

Eq. 2

\[
\frac{G_{\text{art/tum/liv}}}{\text{artBF}_{\text{tum}}/\text{artBF}_{\text{lv}}} = \frac{\text{Slope}_{\text{tum,art}}}{\text{Slope}_{\text{lv,art}}}
\]

Eq. 3

\[
\frac{G_{\text{pv/tum/liv}}}{\text{pvBF}_{\text{tum}}/\text{pvBF}_{\text{lv}}} = \frac{\text{Slope}_{\text{tum,pv}}}{\text{Slope}_{\text{lv,pv}}}
\]

Eq. 4

Fig. 1: Dynamic contrast-enhanced CT examination of a patient with a large colorectal cancer liver metastasis in segment IV before (A) and after contrast injection (B-E). Compared to normal liver parenchyma the lesion clearly is hypervascular in the hepatic arterial phase (B, C) and iso- to hypodense approaching the portal venous phase (D, E). Time-density-curves of the aorta (F), the portal vein (G) and both tumour (H) and normal liver tissue (I) regions-of-interest. CT perfusion values are calculated as the slope of the tissue time-density-curve at the moment of peak enhancement of the reference feeding vessels (respectively hepatic artery and portal vein) divided by the peak enhancement of these vessels. After voxel-by-voxel analysis hepatic artery (J) and portal venous (K) blood flow maps can be created. The high arterial and very low portal venous tumour blood flow compared to normal liver tissue is clearly demonstrated.
DCE-US protocol
The US examinations were performed on a clinically used US apparatus (Aplio Scanner; Toshiba, Japan) equipped with contrast harmonic imaging and quantification software (CHI-Q, Toshiba, Japan). First, a morphologic study was performed in B-mode sonography with a 4.4-MHz C37 convex array transducer. This study allowed us to identify the target lesion and to select the best acoustic window for its assessment. Second, after the injection of a bolus of 2.4 ml microbubble contrast material (Sonovue, Bracco, Italy), which consists of sulphur hexafluoride-filled microbubbles (stable encapsulated gas: perfluorocarbon), at a concentration of 8 μl/ml through a cannula in the left antecubital vein, dynamic image acquisition was performed in breath-hold at maximum inspiration starting 6 sec after contrast injection and lasting at least 30 sec to encompass both hepatic artery and portal venous first-pass maximum-slope of tissue enhancement. The dynamic perfusion measurements were acquired using contrast harmonic imaging with pulse inversion (mechanical index 0.2) using the same 4.4-MHz C37 convex array transducer. To determine the interscan variability a second bolus of 2.4 ml contrast material was administered after a time interval of at least 15 min to allow the effects of the first injection to disappear. All patients were kept under close medical supervision for at least 30 min following the administration. Time-enhancement-curves of normal appearing liver parenchyma and of CRLM were constructed for calculation of perfusion parameters using a dedicated software program (Dynamic Flow, Toshiba, Japan). Time intensity curves constructed from raw linear data of manually drawn ROIs (normal appearing liver parenchyma and as much tumour tissue as visible excluding large visible vessels traversing tumour tissue) were quantified, using automated curve fitting, to extract several indices of perfusion: Cf(A), Cf(B), Cf(AB), H, S, Sn, CV(a) and CV(an):

Curve fitting (Cf):
The start- and endpoint and the saturation value (plateau) are manually drawn on the time-attenuation-curve (Fig. 2). The function used for curve fitting is expressed as follows:

\[ Y = A \left(1-e^{-\frac{t}{Cf(A)}}\right) \]

Cf(A) A value that is correlated with the blood vessel density in a given volume of tissue.
Cf(B) A value that is correlated with the blood inflow velocity.
Cf(AB) Slope at the origin, which is correlated with flow volume.
Fig. 2: The start- and endpoint (A) and the saturation value (plateau) (B) are manually drawn on the time-attenuation-curve for automatic curve fitting (Cf). For calculation of characteristic values (CV) the start- and endpoint as well as the slope calculation range were determined placing vertical lines.

**Characteristic Values (CV):**

The following characteristic values are calculated (Fig. 2):

- **H** The difference between the peak value of the graph and the start point or end point, whichever smaller. In the above example, $H = V_{\text{max}} - V_0$.
- **S** The area under curve of the calculation range.
- **Sn** The normalized “S” obtained by dividing “S” by “H”.
- **CV(a)** Slope value. The slope of the graph within the slope calculation range.
- **CV(an)** The normalized “a” obtained by dividing “a” by “H”.

Presently, the parameter with lowest test-retest variability and highest correlation to therapeutic response for DCE-US based perfusion has not been identified, because of which we calculated all indices, including the afore mentioned perfusion gradient $G$ (Eq. 2-4) in all target lesions. These indices were manually extracted and fractionated into hepatic artery and portal venous perfusion as the time-density curves directly after the inflow of contrast within, respectively, the intrahepatic arteries and portal veins (Fig. 3).
Fig. 3: Dynamic contrast-enhanced US examination of the same patient (A-E), displayed in Figure 1, showing comparable enhancement characteristics. The time-intensity-curves (F) of respectively tumour and normal liver tissue typically show an early peak up-slope during the hepatic arterial phase for tumour tissue and a later peak up-slope during the early portal venous phase for normal liver parenchyma. As is also displayed by the dynamic images the curves intersect: the initially hyper-intense tumours become hypo-intense compared to liver tissue reaching the early portal venous phase.

Statistical analysis:
For determination of the reproducibility of all DCE-US variables we calculated the concordance correlation coefficient (CCC).\textsuperscript{19} Limits of agreement were given as 95\% confidence intervals using the Bland and Altman approach.\textsuperscript{20} CCC values were considered as follows: <0.2 negligible, 0.2–0.4 weak, 0.4–0.7 moderate, 0.7–0.9 strong, and >0.9 very strong correlation.\textsuperscript{21}

For comparison of DCE-US- and DCE-CT-derived indices of perfusion, linear trend analysis was performed using Pearson’s product-moment correlation coefficient ($r$). A subgroup analysis was performed in patients who had received chemotherapy
prior to the dynamic imaging studies. We used an independent samples t-test to test significance of differences.

Results

DCE-CT:
All patients tolerated the DCE-CT protocol well and were able to hold their breath for at least 30 sec. Mean arterial and portal perfusion of normal appearing liver tissue was, respectively, 24.5 ml/min/100 g (range, 10.4–71.1 ml/min/100 g) and 73.6 ml/min/100 g (range, 32.3–172.3 ml/min/100 g). The normal liver tissue was perfused by the hepatic artery for 24% and by the portal vein for 76% on average for the total group (range, 15% - 35% hepatic artery contribution). The mean maximum arterial perfusion in liver metastatic lesions was 34.9 ml/min/100 g (range, 0.0–88.7 ml/min/100 g). The mean maximum portal perfusion in liver masses was -4.0 ml/min/100 g (range, -49.6–54.8 ml/min/100 g), with 16/30 lesions showing a negative slope during peak enhancement of the intrahepatic main portal veins. The false assumption of a negative portal venous flow was caused by the superimposed post-peak dip of the much larger first-pass hepatic artery enhancement, which is often the case in liver tumours.

DCE-US (Fig. 4):
All patients tolerated the microbubble contrast injection well, no adverse reactions were seen. Patients were able to hold their breath for a sufficient amount of time to create first-pass time-density-curves for both the hepatic artery and portal venous perfusion. In two patients with small CRLM (11 mm and 14 mm) only one DCE-US examination was evaluable, since the lesions were not optimally visualized within the contrast mode during first pass passage of contrast material on the second examination.

For the results of all DCE-US-derived perfusion indices, see Tables 1-4. The reproducibility CCC of dynamic US perfusion-derived measurements for normal appearing liver tissue was strong for the slope value CV(a) in calculating both hepatic artery (Table 1; Fig. 4A) and portal venous (Table 2; Fig. 4B) flow (>0.7) and moderate to strong for all other parameters. In comparison with normal liver, CRLM reproducibility was slightly higher (strong in both hepatic artery (Fig. 4C) and portal venous (Fig. 4D) flow for CV(a), Cf(A), Cf(AB), H, and S. In 8 out of 30 patients there was no tumour enhancement at all (Cf(A)<1) and in 9 out of 30 patients the slope of the tumour-time-density curve was negative at the time of peak intrahepatic portal vein enhancement, falsely suggestive for a negative portal venous blood flow. Excluding the non-enhancing tumours,
reproducibility dropped to moderate for all parameters. Reproducibility was 0.70 for the hepatic artery tumour-to-liver perfusion gradient and 0.62 for the portal venous tumour-to-liver perfusion gradient.

Fig. 4: Scatter diagrams showing the test-retest reproducibility of the best scoring DCE-US derived slope-value for hepatic arterial (A, concordance correlation coefficient 0.75) and portal venous (B, concordance correlation coefficient 0.93) blood flow of normal liver parenchyma and hepatic arterial (C, concordance correlation coefficient 0.87) and portal venous (D, concordance correlation coefficient 0.77) blood flow of targeted tumour tissue.

DCE-US versus DCE-CT:

Normal liver parenchyma (Fig. 5A and B):

For normal appearing liver parenchyma, DCE-CT-derived hepatic arterial perfusion values and maximum-slope calculations showed a strong correlation with DCE-US based Cf(A) and CV(a) (r = 0.71 and 0.73, respectively) and moderate correlation with Cf(AB), H and S (r = 0.60, 0.68 and 0.56 respectively). For the portal venous perfusion values correlation was moderate with Cf(A), Cf(AB), S and CV(a) (r = 0.41, 0.62, 0.52 and 0.59, respectively).
Figure 5: Scatter diagrams showing the correlation of dynamic contrast-enhanced US derived perfusion parameter slope values compared to dynamic contrast-enhanced CT derived perfusion values (A, r = 0.73) and portal venous (B, r = 0.40) blood flow of normal liver parenchyma. Tumour tissue (Fig. 5C and D): For tumour tissue the parameters with best correlation between the two techniques were C(A) and C(A) (r = 0.59 for both indices) for the arterial and C(A) (r = 0.59 and 0.50, 0.40 and 0.47, respectively) for the portal venous perfusion. The DCE-CT- and DCE-US-derived arterial tumour-to-liver perfusion gradient G showed a moderate correlation with both the hepatic arterial and the portal venous perfusion (r = 0.59 and 0.57, respectively).

Influence of neo-adjuvant chemotherapy on DCE-US and DCE-CT parameters:

Fourteen (14/30) patients had received chemotherapy regimens prior to the dynamic radiological examinations. For the DCE-CT hepatic arterial and portal venous perfusion values the mean perfusion was significantly different between the no-chemotherapy versus chemotherapy subgroup: 43.9 versus 71.7 ml/min/100 g for the portal venous perfusion (p = 0.04) and 80.3 versus 13.7 ml/min/100 g for the arterial perfusion (p = 0.02) and 13.7 versus 71.7 ml/min/100 g for the portal venous perfusion (p = 0.004). For the DCE-US-derived perfusion indices no significant differences between...
the no chemotherapy versus chemotherapy subgroups were found (p>0.05 for all parameters).

Discussion

This study confirms that a correlation is present between maximum-slope method DCE-CT and microbubble DCE-US derived perfusion parameters. DCE-US can be used as marker for liver tissue and hepatic tumour perfusion. However, the degree of agreement does not validate the interchangeable use of both techniques. Secondly, the interscan reproducibility of DCE-US was not very strong, which means that the technique should be limited for studies where a considerable change in tumour perfusion is to be expected. Furthermore, since many tumours did not show any enhancement at all, DCE-US is not recommended as surrogate marker for response to chemotherapy in patients with liver tumours where tumour perfusion on baseline examination is low. To simplify DCE-US derived perfusion indices and to avoid the influence of biasing parameters such as changes in patients hemodynamic status and fluctuations of first-pass contrast agent concentrations within the feeding vessels, we suggest using the arterial and portal venous perfusion gradient (G) by dividing the maximum slope of tumour tissue by the maximum slope of normal appearing liver parenchyma during peak enhancement of the intrahepatic arteries and portal veins respectively.

Since in both DCE-CT and DCE-US true separation of the hepatic artery and portal venous tissue time-intensity-curves is impossible, the arterial and portal fractions of the liver perfusion can only be estimated. The direct maximum slope method uses the temporal interval between the pre-splenic-peak maximum slope, where hepatic artery contribution is maximum (assuming portal venous contrast inflow and hepatic venous contrast outflow are negligible) and the post-splenic-peak maximum slope, where portal venous contribution is maximum (assuming arterial contrast inflow and hepatic venous contrast outflow reached a plateau and portal venous contribution to the hepatic vein contrast outflow is negligible). The time at which the maximum slope of the portal venous tissue time-enhancement-curve is reached often parallels a post-peak negative slope of the arterial time-enhancement-curve. Although this phenomenon may systematically lead to some underestimation of the portal venous liver tissue perfusion, this is especially clear in regions where arterial perfusion is very high such as rim regions surrounding liver tumours.7,12
The major advantage of DCE-US for the evaluation of novel chemotherapy regimens is that the examination is inexpensive, non-invasive and always rapidly available without adverse effects. Furthermore, the acquisition can easily be repeated (up to six injections of Sonovue (Bracco, Italy) contrast material) for multiple passages within the time-frame of a single examination. According to previous studies the technique has a low intra-observer variability when using time-intensity-curves constructed from raw linear data.

The techniques to quantify tissue perfusion with ultrasound can be divided into non-contrast enhanced high frequency Doppler sonography and dynamic contrast-enhanced low mechanical-index ultrasound such as contrast harmonic imaging using pulse inversion, vascular recognition imaging, combining dynamic doppler sonography with harmonic imaging and pulse subtraction and a technique called replenishment kinetics. In replenishment kinetics time-intensity-curves of novel contrast material influx into the displayed area after destruction (“flash”) of all microbubbles within this area are used for quantification. One major theoretical advantage of this method is the more reliable temporal separation between hepatic artery versus portal venous tissue perfusion using replenishment curves during these distinct phases since replenishment curves return to their starting values in a matter of one or two seconds as opposed to full first-pass enhancement curves which always consist of a mixture of arterial and portal-venous inflow characteristics. In our experience drawbacks of DCE-US techniques are the difficulty in obtaining reliable perfusion values when flow rates are low, the poor depth of penetration when analyzing non-superficial lesions and the fact that it is a single level technique with tumours often showing highly heterogeneous perfusion and histological microvessel density throughout tumour volumes. The latter may be one of the reasons causing the suboptimal test-retest reproducibility found in our study.

When comparing DCE-US derived perfusion indices the slope-value CV(a) (representing the slope of the graph within the slope calculation range) scored best with highest test-retest reproducibility and overall highest correlations to DCE-CT based perfusion values. The suggested perfusion gradient (G), dividing the slope of the tumour tissue by that of normal appearing liver tissue, also showed a high test-retest reproducibility with moderate correlations to the DCE-CT derived perfusion gradient. Since DCE-US techniques do not use arterial or portal venous input functions from a large feeding vessel for reference, this parameter may prove useful as biomarker for response in chemotherapy studies where an effect on the hemodynamic status of the patient is to be expected. Previous studies have shown no effect on normal appearing liver tissue perfusion of administered angiogenesis inhibitors.
The DCE-CT derived arterial & portal venous perfusion values of normal appearing liver tissue are in accordance with other studies. The higher ratio of hepatic artery over portal venous flow in CRLM is also fully comparable to results from other studies. The presented perfusion CT technique and the mathematical model used for quantification also have some important drawbacks: The increase in scan range allows us to scan entire volumes of the liver at the cost of a lower temporal resolution that may cause a decrease in signal-to-noise ratio and the possible scenario of missing an aortic or portal venous peak enhancement during the interscan interval, which can lead to an overestimation of the flow. A theoretical disadvantage of the slope method is the underestimation of the perfusion where the “no venous outflow” assumption is broken. Furthermore, the protocol yields a high effective radiation dose (approximately 24.0mSv). One of the most important advantages of the maximum-slope method is its reproducibility, having a low interscan variability of approximately 13% and a low interoperator variability of about 8%

To conclude DCE-US derived indices of perfusion have a fair test-retest reproducibility and overall show moderate correlation to maximum-slope DCE-CT perfusion values. The techniques cannot be used interchangeably and DCE-US should be limited for studies where a considerable change in tumour perfusion is to be expected and for patients who do not have a low tumour blood flow at baseline. In studies where significant changes of patient’s hemodynamic status are expected we suggest using the perfusion gradient (G) which divides the time-intensity-curve maximum slope of the tumour-tissue by the maximum slope of normal appearing liver parenchyma (excluding the need for an arterial input function).
References


