

nique able to evaluate tumor vascularization. In particular, recently developed quantitative approaches able to measure the amount and the time course of contrast uptake have shown great promise in revealing effective tumour response to anti-angiogenic drugs before tumour changes occur. Aim was to evaluate the feasibility of dynamic CEUS with perfusion software in the quantitative assessment of early vascular effect of Sorafenib in patients with advanced HCC.

**Patients and methods:** Consecutive patients with advanced stage HCC treated with Sorafenib, 400 mg bid, were enrolled in this study. In patients with tumor targets that were accessible to US, CEUS was performed at baseline and after 15 (T1), 30 (T2) and 60 (T3) days. Tumor vasculature was assessed in a specific harmonic mode associated with a perfusion and quantification software (Q-Lab, Philips). Different parameters extracted from the time-intensity curves of contrast uptake were evaluated: peak intensity (PI), time to PI (TPI), area under the curve (AUC), slope of wash in (Pwi), mean transit time (MTT). The percentage variation of US parameters with regards to baseline were calculated and classified as unchanged/increased or decreased values. CEUS results were compared with tumor response evaluated according to RECIST at 2 months, overall survival (OS) and time to progression (TTP).

**Results:** We report the preliminary results obtained in 15 patients treated with Sorafenib. The percentage decrease in several dynamic US parameters at T1 showed a correlation with tumor response in terms of AUC ( $P = 0.006$ ), PI ( $P = 0.014$ ) and Pwi ( $P = 0.029$ ) and with TTP in terms of TPI (0.035) and Pwi ( $P = 0.014$ ). A trend toward correlation with OS was found only for TPI ( $P = 0.070$ ). Changes in tumor vascularisation observed at T1 were always consistent in the same patients at T2 and T3.

**Conclusions:** Dynamic US provide a more reliable and early measure of efficacy for antiangiogenic therapies and could be an excellent tool for selecting patients who will benefit from treatment. However further studies with a greater number of patients are required to confirm these results.

#### P.18.16

##### HEPATIC AND SPLENIC STIFFNESS MEASURED BY TRANSIENT ELASTOGRAPHY: FEASIBILITY AND POSSIBLE ROLE IN PATIENTS WITH HEMOGLOBINOPATHIES

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**Background and aim:** Transient elastography (TE) that measures liver stiffness (LS) is a non-invasive predictor of severe hepatic fibrosis/cirrhosis in chronic liver disease (CLD) and in thalassemic patients. Preliminary studies indicated that also the spleen stiffness measurement (SS) could be useful in CLD patients improving diagnosis of severe liver fibrosis. Present study aimed to both delineate the major determinants of LS and SS and to assess their accuracy as surrogate marker of hepatic fibrosis in haemoglobinopathies.

**Material and methods:** 120 patients with haemoglobinopathic disease were enrolled: 30 had thalassemia major (TM), 74 thalassemia intermedia (TI), 8 thalassodrepanocytosis (TD) and 8 sickle cell disease (SCD). Among them, 6 were excluded due to failure in SS measurement, 114 were included after assessment of both LS and SS using TE (FibroScan, EchoSens, Paris, France); the examinations were considered valid with at least 10 valid measurements, a success rate >60% and an procedures. The test accuracy was evaluated by ROC curve analysis and the inter-observer agreement analyzed by intra-class correlation coefficient.

**Results:** In the 55 splenectomised patients (48%) only LS was obtained, whereas in the other 59 (52%) both LS and SS were available. LS and SS resulted significantly lower in the control group than other ones. The reproducibility was optimal for both LS [0.98 (95% CI 0.95–1)] and SS [0.86 (95% CI 0.80–0.91)]. In TM and TI, LS showed a good diagnostic power both in confirming and excluding severe liver fibrosis/cirrhosis (AUROC 0.93, sensitivity 100%, specificity 70%, LR+4; LR-0.01). At multivariate analysis ALT and PT ratio ( $p < 0.0001$ ) resulted independent determinants of LS, as splenic volume ( $p < 0.0001$ ) for SS. In the subset of HCV-RNA positive TM patients, both LS and SS resulted significantly associated to the stage of hepatic fibrosis.

**Conclusions:** SS is a highly reproducible non-invasive technique with a success rate comparable to that of LS. Both LS and SS values resulted significantly lower in healthy volunteers than in all others pathologic groups. In thalassemic patients LS is an accurate technique to exclude and predict cirrhosis. A strong correlation exists between LS and SS in TM HCV viremic patients. Splenic volume influenced SS, differently from both necroinflammation and hepatic iron overload.

#### P.18.17

##### DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING FOR THE STAGING OF LIVER FIBROSIS: A PRELIMINARY STUDY IN PATIENTS WITH CHRONIC LIVER DISEASE

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**Background and aim:** Liver fibrosis (LF) is often a possible evolution of chronic liver disease, with a significant risk of progression into cirrhosis. This study was designed to establish whether the measurement of apparent diffusion coefficients (ADC) is clinically accurate in diagnosis in a selected series of pts with chronic liver disease (CLD).

**Material and methods:** The study was carried out in the period 2008–2012. We recruited 42 pts with CLD (mean age 53 yrs-range 18–76, 26 M-16 F). Patients were examined using diffusion-weighted magnetic resonance imaging (MRI) with single shot echo-planar technique and with a 1.5 tesla-magnet equipped. This test measures the diffusion of water molecules in the fibrotic liver tissue through the calculation of the ADC that is extracted by the following formula:  $ADC = \ln(S0/S1)/b$ ,  $b=500$ . For each pt the hepatic fibrosis was evaluated in accordance with the METAVIR score (F0-F4) after liver biopsy. Patients were stratified into 3 groups (1, 2, 3) according to the different degree of fibrosis, and the ADC was compared with U-test of Mann-Whitney (U-test). We also evaluated the presence of advanced fibrosis (group 3) or clinically significant fibrosis (groups 2–3) with the use of the analysis Receiver-Operating-Characteristic (ROC).

**Results:** We found a significant difference between group 1 (F0-F1) and group 3 (F3-F4) with  $p=0.0028$ , and between group 2 (F2) and group 3, with  $p=0.026$ . We did not find a significant difference between the ADC values in group 1 and group 2. More widely, a significant difference ( $p=0.001$ ) was observed comparing pts with fibrosis >F2 and pts with fibrosis ≤F2. Area under the curve (AUC) predicted the membership in the group 3 with a value=0.82 (95% CI: 0.657–0.928; cut-off: 1.4154). The sensitivity and specificity were 73.7% and 82.3%, respectively. However, in predicting the membership of clinically significant fibrosis (groups 2–3), we obtained AUC=0.765 (95% CI: 0.595–0.890; cut-off: 1.4154). The sensitivity was reduced to 61.5% and the specificity was 90%.

**Conclusions:** Our study showed a correlation between reduction of ADC and the increasing in liver fibrosis degree. The ADC has appeared useful in staging liver fibrosis in pts with CLD, in particular to distinguish the later stages of fibrosis from early and intermediate stages.

#### P.18.18

##### PRIMARY SCLEROSING CHOLANGITIS IN CHILDREN: A RETROSPECTIVE REVIEW OF TWO ITALIAN CENTERS

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**Background and aim:** Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver disease characterized by inflammation and progressive bile