Title: New methods in the non-invasive diagnosis of liver cirrhosis and portal hypertension

**Background.** Liver cirrhosis is characterized by major changes in liver architecture, including fibrosis and nodules formation. These changes induce alteration of intrahepatic circulation, leading progressively to portal hypertension and liver failure. Therefore, a prompt diagnosis of cirrhosis and portal hypertension is needed in patients with chronic liver diseases.

**Aims.** This work was aimed at identifying new non-invasive methods useful in the diagnosis of cirrhosis and portal hypertension. We hypothesized that two ultrasound parameters, (nodularity of hepatic surface studied by high-frequency transducers and regional hepatic perfusion assessed by the analysis of rupture-reperfusion curves at contrast-enhanced ultrasound -CEUS), might improve the non-invasive evaluation of cirrhosis and portal hypertension.

**Results and conclusions.** Two studies were performed. The first, conducted in patients with clinically suspected cirrhosis, allowed observing that liver surface assessment by high-frequency ultrasound is a simple, cheap and reproducible non-invasive method to diagnose cirrhosis. We quantified of the degree of nodularity by means of the computerized analysis of ultrasound images of liver surface, obtaining a new observer-independent parameter. Moreover, we demonstrated that the combination of liver surface nodularity by US and liver stiffness by transient elastography is superior to both methods to diagnose cirrhosis, decreasing the rate of indeterminate cases and maintaining a high accuracy (over 90% sensitivity and specificity).

The second study, conducted in patients with portal hypertension, showed that the assessment of regional hepatic perfusion (RHP) by the rupture-reperfusion technique of ultrasound contrast by CEUS was safe and easily applicable. This
new method allowed studying hepatic microcirculation in vivo: RHP correlated
with the severity of liver failure and with effective liver perfusion measured by
indocyanine green clearance. RHP changes mirrored changes in hepatic
perfusion after intravenous administration of propranolol, suggesting that this
method might be useful to assess the effect on hepatic perfusion of new drugs
used in portal hypertension.