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Computational analysis to detect resistance mutations to direct acting antivirals in hepatitis C virus

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Hepatitis C virus (HCV) infection is considered as a major public health problem with an estimate of 200 million people infected worldwide. HCV infection is the major cause of chronic liver disease, with severe outcomes including cirrhosis and hepatocellular carcinoma and it is the main cause of liver transplantation. The treatment for HCV chronic infection with pegylated interferon alpha plus ribavirin inhibitors is unspecific; consequently, the treatment is effective in only 50% of patients infected. This has prompted the development of direct-acting antivirals agents (DAA's) that target virus proteins. Unfortunately, since the virus has a high replication rate and its RNA polymerase lacks proofreading activity, genetic variations might produce resistance against the DAA's. These DAA's have demonstrated a potent effect *in vitro* and *in vivo*; however, virus mutations associated with the development of resistance have been described. The objective of this work is to detect mutations in known aminoacids to be implicated in resistance to DAA's in sequences obtained of conventional Sanger and cloning sequencing. We have designed and developed an online information system named Biomedical Mutation Analysis (BMA), which allows users to calculate changes in nucleotide and amino acid sequences for each selected sequence from conventional Sanger and cloning sequencing. BMA allows the computational analysis quickly, easily and effectively. Furthermore, the development of different visualization techniques allows a proper interpretation and understanding of the results. The data obtained from BMA will be useful for HCV resistance surveillance for the design of broad-range inhibitors and rationale therapeutic regimen.

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The role of contrast-enhanced ultrasound in the diagnosis of focal liver lesions

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Introduction: At present, differential diagnosis of focal liver lesions usually identified at computed tomography (CT) or magnetic resonance imaging (MRI). The conventional ultrasound (US) offers no such comparable ability to characterize a focal liver lesion. The appearance of malignant liver lesions in ultrasound B-mode are very variable: they can be hypoechoic, hyperechoic; they can have a peripheral halo. For example, hemangioma and colorectal carcinoma metastases can be very similar and be hyperechoic in a grayscale. New imaging method - contrast enhanced ultrasound (CEUS) with micro bubble contrast agents has improved the ability of US to characterize a focal liver lesions. On CEUS, all liver malignant lesions can present a typical wash-out pattern in the portal and late phases.

Aim: Aim of our study was to evaluate the diagnostic value of CEUS for the characterization of focal liver lesions.

Materials & Methods: This prospective study was carried out at the Petrov Research Institute of Oncology, Ministry of Health, Russia. This study was approved by the institution review board at our institute and informed written consent was obtained from all of the reviewed subjects. 119 patients underwent conventional ultrasound examination including standardized CEUS of a focal liver lesion within our institute. The CEUS results were compared with the CT or MRI. Final diagnosis was based on histology.

Results: CEUS is more sensitive than conventional US for the detection of focal liver lesions. The efficacy of CEUS examination is similar to that of contrast CT and MRI. CEUS may play a significant role in questionable diagnostic situations owing to its ability to visualize characteristic features of different liver lesions therefore, helping to adequately plan the treatment strategy.

Conclusion: It should be noted that the high diagnostic potential of CEUS of focal liver lesions do not decrease the capabilities of the other diagnostic methods (CT and MRI), and in particular cases can supplement them. Therefore, the role of CEUS, in our opinion, should be limited to the use in difficult differential diagnostic cases.

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