RESEARCH – DEVELOPMENT REPORT

Project name: Non-alcoholic fatty liver, viral C hepatitis and gallstone disease – components of the metabolic syndrome. Clinical epidemiology, pathogenesis, non-invasive diagnosis, FINALISM.

Stage IV: The comparative analysis of the invasive and non-invasive methods of the diagnosis and staging of NAFLD. The metabolic component of viral hepatitis C. Pathogenetic mechanism involved in the development of NAFLD and GB. Continuation of the case-control study. Implementation to the hospital software program.

Reported period: 30.10.2007 – 30.05.2008

I.   Activity description:

Key words and descriptors: non-alcoholic fat liver (NAFLD), chronic viral hepatitis C, gallstone disease (GD), Metabolic Syndrome (MS), clinic epidemiology, pathogenic mechanisms, gall bladder motility, software module, data basis.

Activity IV.1:

Activity IV.1 focuses on the the validation of the mathematical modulation techniques and image processing for the confirmative diagnostic and NAFLD staging.

In order to complete this objective, the following actions have taken place:

- The comparative statistic analysis has been carried out for the parameters obtained through the mathematic modulation techniques and image processing and also hepatic morphology on a number of 45 cases of steatosis and 17 witness cases.

- The comparative statistic analysis has been carried out for the parameters through mathematic modulation and image processing and biologic marker (adyponectine) on a number of 33 cases of steatosis and 15 witness cases.

- The elaborated modulation software has been integrated.

- The software modules have been tested at the specialist's office on specific cases.

- Statistic processing has been elaborated on a number of 3005 cases (article accepted and in process of being published, ISI publication).

Activity IV.2

Activity IV.2 had as a target the study of the metabolic component of chronic viral hepatitis C infection.

In this activity the following research have been carried out:

- The virology parameters have been evaluated: viral loading (RNA-HVC) and it was established the meaning for the biologic and morphologic modifications;

- The metabolic parameters have been studied: the glycemic homeostasis, the level insulin in blood, C peptide level, insulin resistance (HOMA-IR);

- The morphologic parameters have been analyzed: hepatic steatosis and fibrosis and the factors associated with these modifications in unilateral and multilateral analysis.

Activity IV.3

Has as target the identification of the pathogenic mechanisms involved in NAFLD and GD:

- The insulin resistance has been evaluated: the glycemic homeostasis, the level insulin in blood, C peptide level, insulin resistance (HOMA-IR);

- An evaluation of the oxidative stress has been carried out through the determination of the serum parameters of the final products of the lipid peroxidase and of the antioxidant protection factors.

- The adipocytokine profile has been evaluated and the correlations with the morphologic and biologic parameters have been determined;

- The witness case study has been continued regarding the association between the investigated factors (NAFLD and GD); therefore it has been elaborated a work processing on a number of 2961 cases.

II.   Results:

- The screening activity has been continued on 8000 patients through ultrasonic methods in order to identify the metabolic profile;

- The mathematic modulation and image processing techniques have been validated so as to confirmatively diagnose and stage the NAFLD;

- The software modules have been elaborated and tested;

- Statistic work have been elaborated;

- The metabolic component of the chronic viral C infection has been investigated through complex biological and morphologic determination;

- Research have been carried out on the pathogenic mechanism involved in the determination of the NAFLD and GD;

- insulin resistance, cytokine profile, oxidative stress;

- The study of the gallbladder motility in GD and MS has been continued;

- The witness case study has been continued (intermediary processing on a number of 2961 cases);

- An intermediary activity report has been accomplished and it includes the technical-economical feedback of the stage.

III.   Expected effects:

- The validation study of the mathematical modulation techniques and image processing specifies the value and the intake of these non-invasive means of diagnosis for the confirmative diagnosis and NAFLD staging;

- The identification of the metabolic component of chronic viral C infection specifies some of the mechanisms that influence the response to the antiviral therapy. Moreover these can become targets of therapeutic actions that lead to the initiation of the treatment;

- Some pathogenic mechanisms that determine NAFLD and GD are being identified and they provide prophylactic and therapeutic perspective;

- The witness case study shows the association between the risk factors and NAFLD and also GD.

The final form of the activity in this stage:

The purposes for this stage have been entirely accomplished in due time. The activities intended for this phase have been finalized by:

- The screening for NAFLD and GD on a hospital population of 8000 patients;

- The validation of the mathematical modulation techniques and image processing for the confirmative diagnosis and NAFLD staging on a number of 45 cases;

- The identification of the metabolic component in chronic viral C infection through a complex morphologic, biologic and virology study;

- The analysis of a pathogenic component involved in determining the NAFLD and GD.

IV.   Published books chapters:

1. M Grigorescu, Corina Radu, M D Grigorescu, Dana Crisan. Hepatita Virală C – Boală metabolică. In: Actualitati in diagnosticul si tratamentul hepatitelor cronice virale. Ed.Medicală Universitară "Iuliu Haţieganu" Cluj Napoca 2008, 18-32.

2. Monica Lupşor, R. Badea, Delia Mitrea, C. Vicaş, S. Nedevschi. Evaluarea şi caracterizarea steatozei, fibrozei şi restructurării parenchimului hepatic cu ajutorul ultrasonografiei şi a metodelor computerizate de analiză a imaginii. In: M. Grigorescu, M.Beuran. Actualităţi în patologia hepatică. Ed.Medicală Universitară "Iuliu Haţieganu" Cluj Napoca 2008, 288 – 302

3. M Grigorescu, Corina Radu. Hepatitele cronice. In: O.Pascu, M. Grigorescu, M. Acalovschi, V. Andreica. Gastroenterologie si Hepatologie - Bazele practicii clinice. Ed. Med Univ Iuliu Hatieganu Cluj-Napoca 2008,467-491.

V.   Published articles:

1. Mircea Grigorescu, Corina Radu, Dana Crişan, Mircea Dan Grigorescu, Alexandru Şerban, Dana Neculoiu, Margareta Rusu, Monica Acalovschi. Metabolic Syndrome, Insulin Resistance and Adiponectin Level in Patients with Chronic Hepatitis C. J Gastrointestin Liver Dis 2008; 17 :147-155.

2. Vicas C, Nedevschi S, Lupsor M, Badea R, Stefanescu H. Fibrosis detection from ultrasound imaging. The influence of necro-inflammatory activity and steatosis over the detection rates. Journal of Automation, Computers, Applied Mathematics 2007; 16 (3): 27-33.

3. Vicas C, Nedevschi S, Lupsor M, Badea R, Grigorescu M. Steatohepatitis Detection from Ultrasound Images Using Attenuation and Backscattering Coefficients. Journal of Automation, Computers, Applied Mathematics 2007; 16 (3): 20-26

4. Monica Lupşor, Radu Badea, Horia Stefănescu, Mircea Grigorescu, Zeno Sparchez, Alexandru Serban, Horatiu Branda, Sorana Iancu, Anca Maniu. Analysis of histopathological changes that influence liver stiffness in chronic hepatitis C. Results from

a cohort of 324 patients. J Gastrointestin Liver Dis 2008; 17 :155-165.

VI.   Articles that appeared in resume volumes:

1. Lupsor M, Badea R, Vicas C, Nedevschi S, Stefanescu H, Tripon S, Suteu T, Radu C, Grigorescu M. Estimating the fibrosis stage in chronic hepatits C patients using image processing methods on ultrasonographic images. Preliminary results. Ultraschall in Med 2007; 28: S1-S74

2. Lupşor M, Stefanescu H, Sparchez Z, Serban A, Grigorescu M, Iancu S, Suteu T, Badea R. The influence of fatty load on liver stiffness in chronic hepatitis C patients. J Hepatol. 2008; 48(supl 2): S278

3. Ofelia Mosteanu, Teodora Atena Pop, Claudia Buzas, Monica Acalovschi. Evaluation of gallbladder motility in patients with non-alcoholic steatohepatitis using real time ultrasonography" 15th United European Gastroenterology Week, 27-31 Octombrie Paris

VII.   Scientific communications:

1. Grigorescu M, Radu C, Lupşor M, Vicaş C, Nedevschi S , Badea R, Spârchez Z, Crisan D, Serban Al. Comparison between attenuation coefficient computed on the ultrasound image and a biological marker, adiponectin, in the diagnosis of steatosis in non-alcoholic fatty liver disease. – lucrare prezentată în cadrul „2008 IEEE International Conference on Automation, Quality and Testing, Robotics AQTR 2008 - THETA 16th edition - May 22-25 2008, Cluj-Napoca, Romania

2. Lupşor M, Badea R, Vicaş C, Nedevschi S, Grigorescu M, Stefănescu H, Radu C, Crişan D, Spârchez Z, Serban Al, Branda H. Ultrasonographic diagnosis of nonalcoholic steatohepatitis based on the quantitative evaluation of the ultrasound beam behavior into the liver – lucrare prezentată în cadrul „2008 IEEE International Conference on Automation, Quality and Testing, Robotics AQTR 2008 - THETA 16th edition - May 22-25 2008, Cluj-Napoca, Romania

3. Lupsor M, Badea R, Mitrea D, Nedevschi S. Evaluarea şi caracterizarea steatozei, fibrozei şi restructurării parenchimului hepatic cu ajutorul ultrasonografiei şi a metodelor computerizate de analiză a imaginii – lucrare prezentată în cadrul simpozionului interuniversitar Cluj-Bucuresti cu tema "Patologia ficatului" organizat in cadrul Clinicii de Chirurgie a spitalului Clinic de Urgenta Bucuresti in perioada 8-10 noiembrie 2007

4. Lupşor M, Stefănescu H, Badea R. Aportul elastografiei tranzitorii unidimensionale (Fibroscan) in evaluarea neinvaziva a hepatopatiilor difuze. - lucrare prezentată în cadrul Seminarului anual al Centrului de Formare în Ultrasonografie, organizat cu ocazia zilelor UMF, 7 dec 2007, Cluj-Napoca

5. Lupşor M, Ştefănescu H, Badea R. Elastografia tranzitorie unidimensională (Fibroscan) – corelaţii cu ecografia convenţională şi cu alte tehnici, în vederea evaluării neinvazive a hepatopatiilor difuze - lucrare prezentată în cadrul Seminarului „Progrese în Ultrasonografie la a V-a ediţie a manifestărilor Maramedica, Baia Mare, 21-23 februarie 2008

6. D. Mitrea, S. Nedevschi, M.Lupsor, R. Badea, "Exploring the Textural Parameters obtained from Ultrasound Images for Modeling the Liver Pathological Stages in the Evolution towards Hepatocellular Carcinoma", of the Proceedings of the 2008 IEEE International Conference on Automation, Quality and Testing, Robotics AQTR 2008 - THETA 16th edition, May 22-25 2008, Cluj-Napoca, Romania

7. Cristian Vicas, Sergiu Nedevschi, Monica Lupsor, Radu Badea, Mircea Grigorescu. Steatohepatitis Detection from Ultrasound Images Using Attenuation and Backscattering Coefficients. *Journal of Automation, Computers and Applied Mathematics* (ACAM), Vol.16, No. 3, pp. 20-26, 2007.

8. Cristian Vicas, Sergiu Nedevschi, Monica Lupsor, Radu Badea, Horia Stefanescu. Fibrosis detection from ultrasound imaging. The role of inflammatory activity and steatosis in detection rates. *Journal of Automation, Computers and Applied Mathematics* (ACAM), Vol.16, No. 3, pp. 27-33, 2007.