

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 V: Conclusions, implementation, release.

Reported period: 30.05.2008 – 10.10.2008

I. Activity description:

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

Activity V.1:

- The aim of this activity is to complete the information synthesis and to elaborate the conclusions.

In order to achieve this aim, the following actions have taken place:

- The statistic analysis has been completed in order to determine the prevalence and to identify the risk factors for NAFLD and GD on the initial number of cases (10089 patients);
- The evaluation of the essential pathogenic components involved in the determination of the metabolic component of C Viral Infection (insulin resistance, adipocytokine profile, steatosis, the iron metabolism) and of NAFLD (insulin resistance, adipocytokine profile, oxidative stress);
- The evaluation of the diagnosis value of the non-invasive biologic markers and the diagnosis value of the innovative image exploration, original comparing to the morphologic invasive exploration.

Activity V.2:

- Had as a target the implementation of the obtained results in the medical practice. In this activity it has been elaborated the course support, and

also a strategy has been set for the screening and diagnosis; moreover, the risk factors for NAFLD and GD have been defined.

Activity V.3: Had as a target the optimization and evaluation of the software applications;

Activity V.4: Large dissemination through presentations and publications. In this activity it has been elaborated: presentations, articles, web page, presentation CDs.

Activity V.5: Dissemination of the presentation CDs and teaching support.

Results:

- The optimization and evaluation of the software applications;
- Statistic processing;
- The determination of the prevalence and the identification of the risk factors for NAFLD and GD through a wide clinic epidemiology study;
- The finalization of the statistic processing in order to identify the metabolic component of chronic viral C infection (hepatic steatosis, insulin resistance, the disturbance of the iron metabolism with complex morphology, biology, virology and imagistic exploration) – see also the final scientific report;
- Complex, comparative analysis of the performance of the invasive and non-invasive diagnosis means of investigation in the chronic viral C infection staging diagnosis (see also – final scientific report);
- Final statistic processing involved in NAFLD determination (insulin resistance, cytokine profile, oxidative stress); see also – final scientific report;
- Final evaluation for the NAFLD invasive and non-invasive means of diagnosis; see also – final scientific report;
- The elaboration of the screening and diagnosis strategy for the NAFLD, in collaboration with ISP;
- Teaching support materials;
- The recommended screening and diagnosis strategy;
- Articles and communications;

- Web page;
- Presentation CD;

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

II. Expected effects:

- The dimensions of the NAFLD and GD might guide the directions of the prophylactic treatment by promoting a certain lifestyle and accomplishing a thorough prophylaxis of the two disease;
- By releasing the information to the family doctors it will be possible to realize a continuous medical education, therefore contributing to the medical information and formation without the extra costs;
- From the economical point of view, through the validation of the non-invasive imagistic and biologic tests and the releasing the results in the field and at a central level (Ministry of Health, National Insurance Company) it will be able to determine an obvious cost deduction by reducing the expensive imported technique dependency and also the expensive invasive exploration with potential complications;
- The optimization of the software leads to a better knowledge of the degree of accuracy and precision with which it is determined the degree of steatosis using the developed software system. Therefore the clinician knows by detail the performances (using terms as sensibility and specify) of the diagnosis instrument;
- The testing the software applications lead to receiving a very important feedback from the doctors, therefore easing and shortening the adaptation and learning period for the medic to this new instrument.

III. 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 finalization for NAFLD and GD on a hospital population of 10089 patients;
- The risk factors identification for NAFLD and GD;
- The synthesis of the information regarding the risk factors for NAFLD and GD;

- The synthesis of the information regarding the metabolic component of chronic viral C infection;
- The synthesis of the information regarding the pathogenic mechanisms of NAFLD (details in the final scientific report);
- The elaboration of the screening and diagnosis strategy for NAFLD;
- The elaboration of a course support;
- The elaboration of articles and communications;
- Completing and multiplying the presentation CD;
- Releasing the information.

IV. Novelty elements:

Published articles:

1. Grigorescu M, Radu C, Lupșor M, Vicaș C, Nedevschi S , Badea R, Spârchez Z, Crisan D, Serban AI. 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 THETA 16th edition, Proceedings Tome III:118-122.
2. Lupșor M, Badea R, Vicaș C, Nedevschi S, Grigorescu M, Ștefănescu H, Radu C, Crișan D, Spârchez Z, Serban AI, Branda H. Ultrasonographic diagnosis of nonalcoholic steatohepatitis based on the quantitative evaluation of the ultrasound beam behavior into the liver. 2008 IEEE International Conference on Automation, Quality and Testing, Robotics AQTR 2008 - THETA 16th edition, Proceedings Tome III:112-117.
3. Lupșor M, Badea R, Vicas C, Nedevschi S, Grigorescu M, Ștefanescu H, Sparchez Z, Radu C, Crisan D, Serban A. Detection of steatosis in chronic hepatitis C, based on the evaluation of the attenuation coefficient computed on the ultrasound image. Medical Ultrasonography 2008; 10 (1): 13-20
4. Radu C, Grigorescu M, Crisan D, Lupșor M, Constatin D, Dina L. Prevalence and associated risk factors of non-alcoholic fatty liver disease in hospitalized patients. J Gastrointest Liver Dis 2008 ;17:255-260.
5. Monica Lupșor, Radu Badea, Cristian Vicaș, Sergiu Nedevschi, Mircea Grigorescu, Horia Ștefănescu, Zeno Sparchez, Horațiu Branda, Corina Radu, Dana Crișan, Alexandru Serban. The diagnosis performance of the attenuation coefficient computed on the ultrasonic image in comparison with the classical ultrasonographic examination, to quantify the hepatic fat content in nonalcoholic steatohepatitis patients. Romanian Journal of Hepatology, (in curs de publicare).
6. S. Nedevschi, C. Vicas, D. Mitrea M. Lupșor, M. Grigorescu, R. Badea, "Usefulness Of Attenuation And Backscattering Coefficients In Investigating Complex Nonalcoholic

Steatohepatitis From Ultrasound Images. Preliminary Results", Proceedings of 19'th Biosignal Conference, 29-30 jun. 2008, Brno, paper ID 126.

Articles appeared in resume volumes:

1. Lupsor M, Vicas C, Nedevschi S, Grigorescu M, Ștefănescu H, Sparchez Z, Serban A, Branda H, Florea M, Badea R. Steatohepatitis Detection from Ultrasound Images Using Attenuation and Backscattering Coefficients. *Ultraschall in Med* 2008; 29: S8
2. Lupsor M, Badea R, Vicaș C, Nedevschi S, Grigorescu M, Ștefănescu H, Spârchez Z, Radu C, Crisan D, Serban Al., Branda H. Diagnosis value of the attenuation coefficient computed from ultrasound image for predicting the presence and severity of nonalcoholic steatohepatitis. *Ultraschall in Med* 2008; 29: S11-S12
3. Lupsor M, Badea R, Ștefănescu H, Sparchez Z, Branda H, Serban A, Grigorescu M, Iancu S. The influence of fatty load on liver stiffness in chronic hepatitis C patients. *Proceedings of the Digestive Disease Week (DDW), San Diego, CA, May 17-22, 2008*
4. Lupsor M, Badea R, Ștefănescu H,, Grigorescu M, Sparchez Z, Branda H Serban A, , Iancu S, Maniu A. Is the steatosis induced by hepatic C virus an influent factor on liver stiffness? *J Gastrointestin Liver Dis.* 2008; 17(supl 1): 123-124
5. Lupsor M, Badea R, Vicaș C, Nedevschi S, Grigorescu M, Ștefănescu H, Sparchez Z, Radu C, Crișan D, Serban A Detection of steatosis in chronic hepatitis C, based on the evaluation of the attenuation coefficient computed on the ultrasound image. *J Gastrointestin Liver Dis.* 2008; 17(supl 1): 247-248

Scientific communications:

1. Grigorescu M. Sindromul metabolic si patologia digestiva. Suior iunie 2008.
2. Lupsor M, Badea R, Ștefănescu H. Evaluarea neinvazivă a hepatopatiilor difuze cu ajutorul elastografiei tranzitorii unidimensionale (Fibroscan®) – lucrare prezentată în cadrul cursului postuniversitar "Actualitati si perspective in patologia infectioasa" organizat cu ocazia celui de-al X-lea Congres național de boli infecțioase cu participare internațională, 4-7 iunie 2008, Cluj- Napoca, Romania
3. Lupsor M, Badea R, Ștefănescu H,, Grigorescu M, Sparchez Z, Branda H Serban A, Iancu S, Maniu A. Is the steatosis induced by hepatic C virus an influent factor on liver stiffness? – lucrare prezentata la sectiunea de prezentari orale la al X-lea Congres de gastroenterologie, hepatologie si endoscopie digestiva, 19-21 iunie 2008, Iasi, Romania
4. Lupsor M, Ștefănescu H. Tehnica elastografică pentru evaluarea afecțiunilor hepatice - lucrare prezentată în cadrul cursului practic de ecografie abdominală organizat cu ocazia celui de-al X-lea Congres de gastroenterologie, hepatologie si endoscopie digestiva, 19-21 iunie 2008, Iasi, Romania
5. Lupsor M. Hepatopatii difuze. Hipertensiunea portală. Fibroza hepatică - lucrare prezentată în cadrul cursului practic de ecografie abdominală organizat cu ocazia celui de-al X-lea Congres de gastroenterologie, hepatologie si endoscopie digestiva, 19-21 iunie 2008, Iasi, Romania
6. Lupsor M, Badea R. Aportul Fibroscan-ului în evaluarea hepatopatiilor cronice difuze. - lucrare prezentată în cadrul mesei rotunde cu tema „Diagnosticul noninvaziv al fibrozei hepatice”, organizata cu ocazia celui de-al X-lea Congres de gastroenterologie,

hepatologie si endoscopie digestiva, 19-21 iunie 2008, Iasi, Romania

7. Sergiu Nedevschi, Cristian Vicas, Monica Lupsor, Radu Badea, Mircea Grigorescu. Usefulness of image processing techniques in assessing the diffuse liver diseases - lucrare prezentata la Workshop on Computers in Medical Diagnoses, organizat cu ocazia 2008 IEEE International Conference on Intelligent Computer Communication and Processing, August 28 - 30, 2008, Cluj-Napoca, Romania

8. Lupsor M, Badea R, Stefanescu H. Posibilitati de optimizare a diagnsoticului neinvaziv al hepatopatiilor difuze prin tehnici ultrasonografice si elastografice – conferinta sustinuta in cadrul ceui de-al XVIII-lea Congres național de hepatologie, Bucuresti, 18-20 Septembrie 2008

9. Grigorescu M. Hepatita cronica virala C: boala virală sau metabolică. Argumente pentru componenta metabolică a infecției virale C: rezistența la insulină in hepatita cronica virala C; contribuția adipocitokinelor în pproducerea steatozei hepatice. Masa rotunda, Simpozionul National de Gastroenterologie,Iasi 19-21 iunie 2008.

10. Radu C. Steatoza hepatică în infecția virală C: prevalență, mecanisme patogenetice. Masa rotunda, Simpozionul National de Gastroenterologie,Iasi 19-21 iunie 2008.

3. Damian D. Diabetul zaharat in infectia virala C. Masa rotunda, Simpozionul National de Gastroenterologie,Iasi 19-21 iunie 2008.

11. Crisan D. Steatohepatita grefata pe infectia virala C. Masa rotunda, Simpozionul National de Gastroenterologie,Iasi 19-21 iunie 2008.

12 Acalovschi M. Infectia cu virus hepatitic C - factor independent de risc pentru litiaza biliară. Masa rotunda, Simpozionul National de Gastroenterologie,Iasi 19-21 iunie 2008.

13. M. Grigorescu. Markerii biologici neinvazuvi in diagnosticul fibrozei hepatice. 2. Radu C. Steatoza hepatică în infecția virală C: prevalență, mecanisme patogenetice. Masa rotunda, Simpozionul National de Gastroenterologie,Iasi 19-21 iunie 2008.

14. Acalovschi M. Patologie nelitiazică a căilor biliare. 2. Radu C. Steatoza hepatică în infecția virală C: prevalență, mecanisme patogenetice. Masa rotunda, Simpozionul National de Gastroenterologie,Iasi 19-21 iunie 2008.

15. Mosteanu O, Pop T, Buyas C, Acalovschi M. Motilitatea veyiculei biliare la pacientii cu ficat gras nonalcoolic. 2. Radu C. Steatoza hepatică în infecția virală C: prevalență, mecanisme patogenetice. Masa rotunda, Simpozionul National de Gastroenterologie,Iasi 19-21 iunie 2008.

Work that has been accepted in future congress:

16. Monica Lupsor, Radu Badea, Horia Ștefănescu, Mircea Grigorescu, Zeno Sparchez, Alexandru Serban, Horatiu Branda, Sorana Iancu, Anca Maniu. Performanța diagnostică a măsurării rigidității hepatice comparativ cu APRI pentru evaluarea neinvaziva a fibrozei. Rezultate pe un lot de 537 pacienți cu infecție virală C. - Al XVIII-lea Congres național de hepatologie, Bucuresti, 18-20 Septembrie 2008 (in curs de publicare)

17. Monica Lupsor, Radu Badea, Cristian Vicaș, Sergiu Nedevschi, Mircea Grigorescu, Horia Ștefănescu, Zeno Sparchez, Corina Radu, Dana Crișan, Alexandru Serban, Mihai Socaciu. Performanța diagnostică a coeficientului de atenuare calculat pe imaginea ecografică în detecția steatozei in hepatita cronica virala C. Rezultate pe un lot de 524 pacienți. - Al XVIII-lea Congres național de hepatologie, Bucuresti, 18-20 Septembrie 2008 (in curs de publicare)

18. „The performance of attenuation coefficient computed on the ultrasound image in quantifying liver steatosis in chronic hepatitis C patients”. Authors: Monica Lupșor, Radu Badea, Cristian Vicaș, Sergiu Nedevschi, Mircea Grigorescu, Horia Ștefănescu, Zeno Sparchez, Corina Radu, Dana Crișan, Alexandru Serban, Mihai Socaciu
16th United European Gastroenterology Week "UEGW 2008"
Vienne, Austria, 18-22 October 2008

19. "Validation of liver stiffness measurement for fibrosis assessment in 419 patients with chronic hepatitis C." Authors: M. Lupsor, R. Badea, H. Ștefanescu, M. Grigorescu, Z. Sparchez, A. Serban, H. Branda, S. Iancu, A. Maniu
16th United European Gastroenterology Week "UEGW 2008"
Vienne, Austria, 18-22 October 2008