

BIOGRAPHICAL SKETCH

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NAME: Jaime (Jaume) Bosch

eRA COMMONS USER NAME (credential, e.g., agency login): BOSCHJ (Role PI, Organization: UNIVERSITAT BERN)

POSITION TITLE: Professor of Medicine

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
1964 I.N.E.M. Girona	Bachiller Ciencias	June 64	
1964-70 Faculty of Medicine, University of Barcelona	MD	June 1970	Medicine
1970-73 University of Barcelona, Faculty of Medicine. 1973	PhD		Liver- Hepatorenal Sd
1970-79 Hospital Clínic, University of Barcelona Board Certified	Internal Medicine	July 1975	
Board Certified	Gastroenterology	July 1979	Hepatic Hemodynamics (Dr RJ Groszmann)
1980-82 Yale University, New Haven CT			

A. Personal Statement

I have been involved in the study of portal hypertension over the past 4 decades. Over this time, I established a world renowned Hepatic Hemodynamic Laboratory at the University of Barcelona Hospital Clinic and more recently at the Inselspital, University of Bern. My work in portal hypertension has encompassed from generating animal models for cirrhosis, study its pathophysiology, establishing new therapeutic targets and developing new treatments (several of them recommended by current guidelines), as well as innovating the evaluation of portal hypertension. Within this last item, my team has made seminal contributions regarding the use of the hepatic vein pressure gradient (HVPG), including its standardization, clinical applicability, correlation with clinical events and prognostic value in chronic liver diseases, together with the development of non-invasive tools for the assessment of portal hypertension, including ultrasound (US), contrast enhanced (CE) US, transient elastography and combinations of these. Since 2004 I have cooperated with Prof Berzigotti in the study and development of ultrasound based new non-invasive methods for portal hypertension. Consequently, I am highly qualified to be a robust partner in the current research proposal aimed at establishing the utility of SHAPE in the management of portal hypertension.

B. Positions and Honors**Positions and Employment**

1979-1985 Faculty member, Liver Unit, Hospital Clinic, University of Barcelona
 1980-1985 Associate Professor of Medicine, University of Barcelona,
 1985-2012 Chief of Section, Liver Unit and Hepatic Hemodynamic Lab, Hospital Clinic, Barcelona
 1985-2017 Professor of Medicine, University of Barcelona, School of Medicine
 1995-1998 General Manager, National Research Program for Health and Pharmacy, Inter-ministerial
 Commission for Science and Development, Government of Spain
 1999/08-2000/02 Visiting Professor of Medicine, Yale University, New Haven CT, USA
 1999-2003 Chief of the Liver Unit, Hospital Clínic, University of Barcelona
 2003-2017 Chair of Medicine, University of Barcelona, Faculty of Medicine

2006-2015	Scientific Director, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (Ciberehd), Ministry of Science and Innovation.
2015-present	Guest Professor of Medicine, Department of Biomedical Research, Bern University, Hepatology, University Clinic for Visceral Surgery and Medicine, Inselspital.
2016-present	Chairman, International Baveno Cooperation Consortium
2017-present	Emeritus Professor of Medicine, University of Barcelona, Spain.

Honors

1970	Best graduate of the Medical School, University of Barcelona, Caixa de Pensions Award.
2006	Special Recognition Award, European Association for the Study of the Liver
2008	Recognition Award to Excellence in Medical Research, Catalan College of Physicians.
2012	Gold Medal, Canadian Association for the Study of the Liver.
2013	Best Scientist in Spain: Medical Research. Lilly Foundation
2014	Doctor Honoris Causa in Medical Sciences, University Paul Sabatier, Toulouse, France
2016	Elected Fellow of the Royal College of Physicians (FRCP), London.
2016	Elected Fellow of the American Association for the Study of Liver Diseases (FAASLD)
2016	Doctor Honoris Causa in Medical Sciences, University of Cluj-Napoca, Romania
2017	Special Recognition Award for Lifetime Achievements, Spain Association for the Study of the Liver
2020	Elected Honorary President, EASL International Liver Congress

C. Contributions to Science

- 1. New animal models of portal hypertension:** I was directly involved in the development of chronic bile duct ligation (CBDL) as a quick model of cirrhosis leading to the complications of portal hypertension, which has been widely used thereafter (489 papers in PUBMED under [chronic bile duct ligation] AND [portal hypertension OR cirrhosis]). I also developed a rat model of variceal hemorrhage, and more recently my team has established a model of NASH with advanced fibrosis and cirrhosis.
 - Bosch J, Enriquez R, Groszmann RJ, Storer EH. Chronic bile duct ligation in the dog: hemodynamic characterization of a portal hypertensive model. *Hepatology*. 1983;3(6):1002–1007. doi:10.1002/hep1840030618
 - Castañeda B, Debernardi-Venon W, Bandi JC, Andreu V, Pérez-del-Pulgar S, Moitinho E, Pizcueta P, Bosch J. The role of portal pressure in the severity of bleeding in portal hypertensive rats. *Hepatology*. 2000 Mar;31(3):581-6. doi: 10.1002/hep.510310306. PMID: 10706546.
 - Morales J, Moitinho E, Abrales JG, Fernández M, Bosch J. Effects of the V1a vasopressin agonist F-180 on portal hypertension-related bleeding in portal hypertensive rats. *Hepatology*. 2003;38(6):1378–1383. doi:10.1016/j.hep.2003.09.023
 - Maeso-Díaz R, Boyer-Díaz Z, Lozano JJ, Ortega-Ribera M, Peralta C, Bosch J, Gracia-Sancho J. New Rat Model of Advanced NASH Mimicking Pathophysiological Features and Transcriptomic Signature of The Human Disease. *Cells*. 2019 Sep 10;8(9):1062. PMID: 31510105
- 2. Advances in the pathophysiology of portal hypertension:** A better knowledge of the pathophysiology of portal hypertension has been paramount in improving its treatment. In that regard, my team was the first in showing the importance of nitric oxide (NO) in the hyperkinetic circulation as well as demonstrated the importance of hyperglucagonism and angiogenesis in portal hypertension, and defined the mechanisms of endothelial dysfunction and increased hepatic vascular tone.
 - Pizcueta P, Piqué JM, Fernández M, Bosch J, Rodés J, Whittle BJ, Moncada S. Modulation of the hyperdynamic circulation of cirrhotic rats by nitric oxide inhibition. *Gastroenterology*. 1992 Dec;103(6):1909-15. doi: 10.1016/0016-5085(92)91451-9. PMID: 1451984.
 - Fernández M, Semela D, Bruix J, Colle I, Pinzani M, Bosch J. Angiogenesis in liver disease. *J Hepatol*. 2009 Mar;50(3):604-20. doi: 10.1016/j.jhep.2008.12.011. Epub 2008 Dec 31. PMID: 19157625.
 - Marrone G, Maeso-Díaz R, García-Cardena G, Abrales JG, García-Pagán JC, Bosch J, Gracia-Sancho J. KLF2 exerts antifibrotic and vasoprotective effects in cirrhotic rat livers: behind the molecular mechanisms of statins. *Gut*. 2015 Sep;64(9):1434-43. doi: 10.1136/gutjnl-2014-308338. Epub 2014 Dec 10. PMID: 25500203.

- Tripathi DM, Vilaseca M, Lafoz E, Garcia-Calderó H, Viegas Haute G, Fernández-Iglesias A, Rodrigues de Oliveira J, García-Pagán JC, Bosch J, Gracia-Sancho J. Simvastatin Prevents Progression of Acute on Chronic Liver Failure in Rats With Cirrhosis and Portal Hypertension. *Gastroenterology*. 2018 Nov;155(5):1564-1577. doi: 10.1053/j.gastro.2018.07.022. Epub 2018 Jul 25. PMID: 30055171.

3. Development of new treatments for portal hypertension: As a successful translational research, after its characterization in the bench, my team has introduced in clinical practice treatments for portal hypertension that are recommended by current guidelines, including new indications for beta-blockers, use of terlipressin, somatostatin and pre-emptive TIPS in variceal bleeding, combination therapy, and introduction of simvastatin for cirrhosis. Among the many RCT's that I directed or co-directed, I selected:

- Groszmann RJ, Garcia-Tsao G, Bosch J, et al. Beta-blockers to prevent gastroesophageal varices in patients with cirrhosis. *N Engl J Med*. 2005;353(21):2254–2261. doi:10.1056/NEJMoa044456
- García-Pagán JC, Caca K, Bureau C, Laleman W, Appenrodt B, Luca A, Abraldes JG, Nevens F, Vinel JP, Mössner J, Bosch J; for the Early TIPS (Transjugular Intrahepatic Portosystemic Shunt) Cooperative Study Group. Early use of TIPS in patients with cirrhosis and variceal bleeding. *N Engl J Med*. 2010 Jun 24;362(25):2370-9. doi: 10.1056/NEJMoa0910102. PMID: 20573925.
- Garcia-Tsao G, Abraldes JG, Berzigotti A, Bosch J. Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases [published correction appears in *Hepatology*. 2017 Jul;66(1):304]. *Hepatology*. 2017;65(1):310–335. doi:10.1002/hep.28906
- Villanueva C, Albillos A, Genescà J, Garcia-Pagan JC, Calleja JL, Aracil C, Bañares R, Morillas RM, Poca M, Peñas B, Augustin S, Abraldes JG, Alvarado E, Torres F, Bosch J. β blockers to prevent decompensation of cirrhosis in patients with clinically significant portal hypertension (PREDESCI): a randomised, double-blind, placebo-controlled, multicentre trial. *Lancet*. 2019 Apr 20;393(10181):1597-1608. doi: 10.1016/S0140-6736(18)31875-0. Epub 2019 Mar 22. Erratum in: *Lancet*. 2019 Jun 22;393(10190):2492. PMID: 30910320.

4. Use of the hepatic vein pressure gradient (HVPG) as a measurement of portal pressure. My team has extensively investigated the use of HVPG in the evaluation and management of portal hypertension, including the better use of the technique, clinical applicability, correlation with clinical events, prognostic value and its use monitoring and guiding therapy of portal hypertension.

- Feu F, García-Pagán JC, Bosch J, et al. Relation between portal pressure response to pharmacotherapy and risk of recurrent variceal haemorrhage in patients with cirrhosis. *Lancet*. 1995;346(8982):1056–1059. doi:10.1016/s0140-6736(95)91740-3
- Ripoll C, Groszmann R, Garcia-Tsao G, Grace N, Burroughs A, Planas R, Escorsell A, Garcia-Pagan JC, Makuch R, Patch D, Matloff DS, Bosch J; Portal Hypertension Collaborative Group. Hepatic venous pressure gradient predicts clinical decompensation in patients with compensated cirrhosis. *Gastroenterology*. 2007 Aug;133(2):481-8. doi: 10.1053/j.gastro.2007.05.024. Epub 2007 May 21. PMID: 17681169.
- Bosch J, Abraldes JG, Berzigotti A, García-Pagan JC. The clinical use of HVPG measurements in chronic liver disease. *Nat Rev Gastroenterol Hepatol*. 2009;6(10):573–582. doi:10.1038/nrgastro.2009.149
- La Mura V, Garcia-Guix M, Berzigotti A, Abraldes JG, García-Pagán JC, Villanueva C, Bosch J. A new prognostic algorithm based on stage of cirrhosis and HVPG to improve risk-stratification after variceal bleeding. *Hepatology*. 2020 Jan 20;10.1002/hep.31125. doi: 10.1002/hep.31125. Epub ahead of print. PMID: 31960441.

5. Development of non-invasive tools for the assessment of portal hypertension: These include development of a non-invasive tool for endoscopic measurements of variceal pressure, the use of Doppler-ultrasound (US), of contrast enhanced (CE) US, and transient elastography, alone and in combination. Our group studied dynamic contrast-enhanced ultrasound (DCE-US) to visualize and model the hepatic microcirculation and the resulting network graph modelling of properties based on DCE-US closely mirrors fibrosis and portal hypertension. This project set the background for an international project that has been funded by the European Commission (CLEVER Project; Industry-Academia Partnerships and Pathways

(IAPP) FP7-PEOPLE-2013-IAPP, Grant agreement no.: 612273; 2013-2017). These are in direct relationship with the present work, and further support our appropriateness for the current proposal.

- Berzigotti A, Nicolau C, Bellot P, Abraldes JG, Gilibert R, García-Pagan JC, Bosch J. Evaluation of regional hepatic perfusion (RHP) by contrast-enhanced ultrasound in patients with cirrhosis. *J Hepatol.* 2011 Aug;55(2):307-14. doi: 10.1016/j.jhep.2010.10.038. Epub 2010 Dec 15. PMID: 21167236.
- Berzigotti A, Seijo S, Arena U, Abraldes JG, Vizzutti F, García-Pagán JC, Pinzani M, Bosch J. Elastography, spleen size, and platelet count identify portal hypertension in patients with compensated cirrhosis. *Gastroenterology.* 2013 Jan;144(1):102-111.e1. doi: 10.1053/j.gastro.2012.10.001. Epub 2012 Oct 8. PMID: 23058320.
- Procopet B, Berzigotti A, Abraldes JG, Turon F, Hernandez-Gea V, García-Pagán JC, Bosch J. Real-time shear-wave elastography: applicability, reliability and accuracy for clinically significant portal hypertension. *J Hepatol.* 2015 May;62(5):1068-75. doi: 10.1016/j.jhep.2014.12.007. Epub 2014 Dec 13. PMID: 25514554.
- Abraldes JG, Bureau C, Stefanescu H, Augustin S, Ney M, Blasco H, Procopet B, Bosch J, Genesca J, Berzigotti A. Noninvasive tools and risk of clinically significant portal hypertension and varices in compensated cirrhosis: The "Anticipate" study. *Hepatology.* 2016 Dec;64(6):2173-2184. doi: 10.1002/hep.28824. Epub 2016 Oct 27
- Berzigotti A, Piscaglia F, Amat-Roldan I, Gilibert R, Procopet B, Stefanescu H, Bilbao I, Sansone V, Allegretti G, Lens S, Garcia-Pagan JC, Bosch J, on behalf of the CLEVER Study investigators. Non-invasive measurement of HVPG using graph analysis of dynamic contrast-enhanced ultrasound: the CLEVER Study. *J Hepatol* 2018; 68:S76.

Complete List of Published Work: Last 200 publications in MEDLINE (from 2010) in My Bibliography:

<https://www.ncbi.nlm.nih.gov/myncbi/jaime.bosch.1/bibliography/public/>

Full list of publications in Pubmed: [Bosch J AND liver] [Bosch J AND portal]

D. Additional Information: Research Support and/or Scholastic Performance

Dr J.Bosch has obtained continued support for his research through national and international funding agencies, including the Fondo de Investigación Sanitaria (FIS), Instituto de Salud Carlos III, Ministry of Health and of Economy and Innovation; Plan Nacional de Salud, Ministry of Universities and Research; NIH and European Commission. The last grants received are listed below:

Ongoing Research Support

- Bern Center for Precision Medicine Grant 2019 09/01/19-09/01/20
Predictive factors of cirrhosis regression in patients with advanced chronic liver disease.
The major goal of this pilot project is to investigate –omics technologies patients with regression of liver cirrhosis vs. patients without evidence of cirrhosis regression after removal of the etiological cause.
Role: Co-InvestigatorI (with Berzigotti, A)
- Swiss National Science Foundation 320030_189252 (Berzigotti & Gracia-Sancho) 11/01/19-10/31/22
Inhibition of the stiffness-derived molecular axis to improve liver cirrhosis and portal hypertension
The major goal of this project is to study the effect of the stiffness of extracellular matrix on the biology of liver cells (hepatocyte, hepatic stellate cells, sinusoidal endothelium cells) as potential novel target of therapy in advanced liver disease. Role: Co investigator

Completed Research Support (selected)

- European Commission FP7-PEOPLE-2013-IAPP, 612273 (Bosch) 10/01/13-10/01/17
Contrast-enhanced uLtrasound for livEr-disease eVAluation: development and validation of a novel E-Health-software for Risk-stratification- CLEVER
The goal of this project was to test the graph analysis of images obtained by dynamic contrast-enhanced ultrasound as potential new method to assess portal hypertension. Role: PI

- Ministerio de Economía y Competitividad PI13/00341 (Bosch J) 01/01/2014 - 31/12/2016
 Hemodinámica hepática e hipertensión portal en la cirrosis. Avances en la fisiopatología y tratamiento (Estudios clínicos y experimentales).
 Project devoted to the study of the pathophysiology of the increased hepatic resistance in cirrhosis with the aim of discovering new therapeutic targets. Role: PI
- Ministerio de Ciencia e Innovación LIVERBIOMARK (Bosch J) 01/10/2010 - 31/12/2013
 Desarrollo de biomarcadores del grado de fibrosis hepática y del pronóstico de pacientes con enfermedades hepáticas avanzadas mediante el uso de herramientas metabolómicas.
 Project for developing metabolomics biomarkers of fibrosis progression in advanced chronic liver disease. Role: PI
- Ministerio de Ciencia e Innovación PS09/01261 (Bosch J) 01/01/2010 - 31/12/2013
 Hepatic hemodynamics and portal hypertension in cirrhosis. Advances in the pathophysiology, non-invasive evaluation and therapy. (Clinical & experimental studies) Role: PI
- Ministerio de Educación y Ciencia EC08/00091 (Bosch J) 01/01/2009 - 30/06/2013
 Estudio multicéntrico, aleatorizado, doble-ciego, controlado con placebo, sobre la eficacia del tratamiento de beta-bloqueantes para prevenir la descompensación de la cirrosis con hipertensión portal (Estudio PREDESCI)
 Project devoted to perform a double-blind randomized controlled trial on the use of non-selective beta-blockers for preventing the first clinical decompensation in patients with advanced chronic liver disease (PREDESCI Study). Role: PI