CURRICULUM VITAE

Jacques OHAYON, Ph.D. , Professor of Mechanics

Office Chambéry
University of Savoie
Engineering School Polytech Annecy-Chambéry
Mechanics and Material Department
73376 Le Bourget du Lac - Cedex - France
Email : Jacques.Ohayon@univ-savoie.fr
Tél. 04 79 75 86 04 - Fax : 04 79 75 86 65

Office Grenoble
Laboratory Techniques for Biomedical Engineering and Complexity Management - Informatics, Mathematics and Applications (TIMC-IMAG) - CNRS UMR 5525 - *Cellular and Tissular Dynamics & Functional Microscopy Team*
University Joseph Fourier, 38706 La Tronche, France.
Email : Jacques.Ohayon@imag.fr
Tél. : 04 56 52 01 24 - Fax : 04 56 52 00 22
http://membres-timc.imag.fr/Jacques.Ohayon/

Personal Data

Date of Birth:	December 17, 1958 *(55 years old)*
Marital Status:	Married, four children (23, 21, 21 and 14 years old)
Citizenship:	France

Education

♦ 1992	Habilitation in Mechanics and Robotics, University of Paris 12 Val-de-Marne (UPVM), France
♦ 09/1985-09/1988	Post-Doctoral Fellow with Dr. Richard S. Chadwick at the Mechanical Engineering Section, National Institutes of Health (NIH), Bethesda, Maryland, USA.
♦ 1985	Ph.D. Mechanical Engineering, University of Paris 12 Val-de-Marne (UPVM), France
♦ 1982	M.Sc of Biomechanical Engineering, Compiègne University of Technology (UTC), France

Professional Appointments

♦ Since 9/93	Full Professor of Mechanics - University of Savoie, Engineering School Polytech Annecy-Chambéry, France
♦ 12/06-12/07	Sabbatical as Senior Visiting Scientist at the National Institutes of Health (NHLBI-NIH), Bethesda, MD, USA
♦ 09/98-09/01	Director of the Composite Material Dept. of the Engineering School Polytech Annecy-Chambéry, France
♦ 09/92-09/93	Director of the Science Adult training at the University of Paris 12 Val-de-Marne (UPVM), France
♦ 12/88	Associate Professor of Mechanics at the University of Paris 12 Val-de-Marne (UPVM), France

Awards, Honors and Scientific recognitions

- ♦ Prize of the National Society of Biomechanics for my research on Cardiac Mechanics of the Left Ventricle, Bruxelles 1988
- ♦ Recognition of the European Society of Biomechanics for our work performed with my Post-doctoral fellow Simon Le Floc'h on elasticity reconstruction of atherosclerotic plaques - Edinburgh, UK, 5-8 July 2010
- ♦ Recognition of the excellence of my research in biomechanics by the French national comity of universities (PES, CNU 60ème section), October 2011
- ♦ Recognition of the Mechanical Doctoral School of Grenoble University (UJF) for our work performed with my Ph.D. student Nicolas Mesnier on Biomechanics of Atherosclerotic Plaque Growth, Grenoble, 28 November, 2012

International Invited Lectures, Seminars and Workshops

- ♦ Swiss Federal Institute of Technology (EPFL), invited by Professor Jean-Jacques Meister, Director of the Biomedical Engineering Laboratory, Ecublens, Switzerland, April **1999**
- ♦ University of Montréal, invited by Professor Guy Cloutier, Director of the Laboratory of Biorheology and Medical Ultrasonics, Montreal, Canada, June **2003**
- ♦ University Polytechnic of Madrid, invited by Professor José M. Goicolea, Madrid, Spain, October **2003**
- ♦ University of Montréal, invited by Professor Gilles Soulez Notre Dame Hospital, Montréal, Canada, June **2004**
- ♦ Invited by Professor E. Onate to the 6th European Framework Program comity, Bruxelles, Belgium, November **2004**
- ♦ University of Montréal, invited by Professors Gilles Soulez and Guy Cloutier, Montréal, Canada, March **2005**
- ♦ National Heart Lung Blood Institute (NHLBI) at the National Institutes of Health (NIH), invited by Dr Richard S. Chadwick, Bethesda, MD, USA, April **2005**
- ♦ National Institute of Biomedical Imaging and Bioengineering (NIBIB) at NIH, invited by Dr Roderic I. Pettigrew, Bethesda, MD, USA, April **2005**
- ♦ University of Montréal, invited by Professors Gilles Soulez and Guy Cloutier, Montréal, Canada, February **2006**
- ♦ Invited by the Spanish Ministry of Research and Innovation to perform series of 10 seminars to researchers of universities of Zaragoza, Madrid, Barcelona, Valence; University of Zaragoza, Spain, March **2006**
- ♦ 5th World Congress of Biomechanics, Invited by Professor D. Stamenovic, Munich, Germany, August **2006**
- ♦ 5th World Congress of Biomechanics, Invited by Professors G. Holzapfel et T. Matsumoto, Munich, Germany, August **2006**
- ♦ Invited by the Spanish Ministry of Research and Innovation to perform series of 8 seminars to researchers of universities of Zaragoza, Madrid, Barcelona, Valence; University of Zaragoza, Spain, April **2008**
- ♦ 4th International symposium on Biomechanics in Vascular Biology and Cardiovascular Disease, invited by Dr F. Gijsen, Rotterdam, Netherlands, April **2009**

- Invited by Dr R.I. Pettigrew Director of the National Institute of Biomedical Imaging and Bioengineering (NIBIB) at NIH, to participate at a international workshop regrouping 15 MD and Ph.D experts on Atherosclerotic Plaque. Working Group meeting, NIH-HHLBI, Bethesda, Maryland, USA, June **2009**
- University of Barcelona, invited by Professor Petia Radeva Director of the Computer Vision Center, Spain, April 2010
- 7th International symposium on Biomechanics in Vascular Biology and Cardiovascular Disease, invited by Professors F. Gijsen and J. Oshinski, Atlanta, USA, April **2012**
- Invited by Drs A.M. Gharib and R.I. Pettigrew, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) at NIH, December **2012**
- Invited by Professor Sheldon Weinbaum, City College of New York, Biomedical Engineering Dept, USA, December **2012**
- Invited by Dr Saami K Yazdani, University of South Alabama, Mechanical Engineering Dept, USA, March **2013**
- Invited by Dr Anton van der Steen, Erasmus MC, University Medical Center, Rotterdam, Netherlands, October **2013**
- Invited in **2013** by the editors of 3 international journals (***Journal of Biomechanics***, ***Annals of Biomedical Engineering***, ***Computerized Medical Imaging and Graphics*****)** to publish in their special issue journal on " *Atherosclerotic Plaque*".
- 7th World Congress of Biomechanics, Invited by Professors T. Matsumoto, Boston, USA, July **2014**
- 7th World Congress of Biomechanics, Invited by Drs J. Humphrey, F. Gijsen to **chair a session on "*Mechanobiology and Atherosclerotic Plaque Composition*"**, Boston, MA, USA, July **2014**.

Research Grants and Scientific Animations

International Grants

♦ "Grid based decision support system for assisting clinical diagnosis and interventions in cardiovascular problems (DISHEART)" (Co-Investigator), European Project CRAFT 2004-2006, 6th Framework Program (Coordinator: Pr. E. Onate, CIMNE, Barcelona, Spain)

♦ "Modulography and elastography of arteries: Non invasive and invasive approaches (MELANII)". Principal Investigators: J. Ohayon (France) and G. Cloutier (Canada). ANR/CRSNG INTERNATIONAL FRANCE/CANADA Project 2010-2013

National Grants

♦Regional Rhône-Alpes Grant 2005-2008 (Principal Investigators: J. Ohayon and G. Finet). "In vivo mechanical characterization of atherosclerotic plaque", with a 3-year PhD student grant for Simon Le Floc'h

♦ "Biomechanics of atherosclerotic plaque and residual stresses (ATHEBIOMECH)". Principal Investigators: D. Fagret and J. Ohayon (France). French Research National Agency (ANR) Project 2006-2009

Advisor of the following Ph.D. Students since *2007*

♦2004-2007 : *M. Thomas Boudou* - Thèse EDISCE-UJF (France) ♦2006-2009 : *M. Alain Kamgoué* - Thèse EDISCE-UJF (France). ♦2006-2009 : *M. Simon Le Floc'h* - Thèse EDISCE-UJF (France) ♦2007-2011 : *M. Nicolas Mesnier* - Thèse IMEP2-UJF (France) ♦2007-2012 : *Mme Julie Héroux* - Thèse EDISCE-UJF (France/USA) ♦2010-2013 : *Mme Adeline Bouvier* - Thèse EDISCE-UJF (France) ♦2010-2013 : *M. Flavien Deleaval* - Thèse EDISCE-UJF (France) ♦2013-2016 : *M. Antoine Tacheau* - Thèse EDISCE-UJF (France). ♦2013-2016 : *M. Benoit KALMAN* - Thèse IMEP2-UJF (France).

Sabbatical of Researchers Performed in my Group DyCTiM-TIMC-CNRS-UJF-Grenoble

♦2011: Sabbatical of Professor Guy Cloutier, Director of the Laboratory of Biorheology and Medical Ultrasonics, University of Montreal, Canada (3 months)

♦2007: Sabbatical of Professor Estefania Pena, from the Mechanical Engineering Department of the University of Zaragoza, Spain (3 months)

In Charge of an International Interdisciplinary Consortium on Biomechanics of Atheroscletic Plaque

On 2006, I was personally invited by Dr R.I. Pettigrew, Director of the National Institute of Biomedical Imaging and Bioengineering (NIBIB) at NIH, Bethesda MD - USA (*http://www.nibib.nih.gov/About/Directories/Pettigrew*), to spend one year (as a senior visiting scientist) in his laboratory to create, animate and coordinate an interdisciplinary international consortium on Biomechanics of Atherosclerosis regrouping experts in Radiology, Cardiology, Biology, Mechanics, Mathematics, Pathology and Image analysis. This international consortium that I coordinate since 2007 and with which we already published together more than 36 studies, is composed of: National Institutes of Health (NIH), **USA** (Drs R.I. Pettigrew, MD, PhD and A.M. Gharib, MD, CT and MRI Imaging experts) - University of Montréal, **Canada** (Drs G. Cloutier, PhD and G. Soulez, MD, PhD, MRI imaging and Ultrasound experts, respectively) - University of Tohoku, **Japan** (Dr S. Yoshifumi, MD, PhD, Acoustic Microscopy expert) - University of Zaragoza, **Spain** (Drs M. Malvé, PhD, M.A. Martinez, PhD Applied Fluid and Solid Mechanics experts) - EPFL University of Lausanne, **Switzerland** (Dr. M. Stuber, PhD, MRI expert)- University of South Alabama, **USA** (Dr. S. Yazdani, PhD, Tissue Engineering expert) - University of Lyon, **France** (Drs. G. Rioufol, MD, PhD and G. Finet, MD, PhD, IVUS and OCT Imaging experts) - University of Grenoble, **France** (Dr. L. Riou, PhD, Biology expert) - University of Rochester, NY, USA (Dr. M.M. Doyley, PhD, Applied Physics and Mathematics expert).

In Charge of an International France/USA/Canada Experimental Ultrasound Platform for Intravascular Investigations

The international France/USA/Canada ultrasound research platform for intravascular explorations that I created and developed since 2009 is composed of one Galaxie II IVUS-40Mhz system from Boston Scientific (image precision close to 150 µm), one optical coherence tomography system (image precision close to 20 µm) from Lightlab Imaging, and the last IVUS-60Mhz system of Silicon Valley Medical Instrument with an image precision close to 60µm.

My actual h-index is **19** - This h-index was extracted from the Web of Science on November 30, 2013 (see page 3 for Citations and Published items reports of the latest 20 years)

VII. LISTE DES TRAVAUX ET DES PUBLICATIONS / PERSONAL BIBLIOGRAPHY

International articles	61	National conferences (with Proceedings)	36
French national articles	18	International conferences (with Abstracts)	24
Book chapters	21	National conferences (with Abstracts)	7
International conferences (with Proceedings)	60	Patents	4
h-index = 19 *(from the Web of Science, November 30, 2013)*			

Articles Soumis à des Comités de lecture Publiés dans des Revues Internationales (n=61)

Peer-Reviewed International Journal Articles (n=61)

13-1a Majdouline Y, **Ohayon J**, Keshavarz-Motamed Z, Roy Cardinal MH, Garcia D, Allard L, Lerouge S, Soulez G, Cloutier G. Endovascular shear strain elastography can detect and characterize the severity of atherosclerotic plaques: In vitro and in vivo validations, ***Ultrasound in Medicine and Biology***, (in press), 2013.

13-2a **Ohayon J**, Finet G, Le Floc'h S, Cloutier G, Gharib AM, Heroux J, Pettigrew RI. Biomechanics of atherosclerotic plaque: Sites, Stability and in vivo elasticity modeling. ***Ann Biomed Eng,*** Special issue paper, (in press), 2013.

13-3a Riou LM, Broisat A, Ghezzi C, Finet G, Rioufol G, Gharib AM, Pettigrew RI, **Ohayon J**. Effects of Mechanical Properties and Atherosclerotic Artery Size on Biomechanical Plaque Disruption - Mouse versus Human, ***J of Biomech***, Special issue paper, (in press), 2013.

13-4a Mercure E, Destrempes F, Roy Cardinal MH, Porée J, **Ohayon J**, Soulez G, Cloutier G, Processing steps and local compensation of ultrasound beam misalignment for non-invasive vascular axial strain computations on carotid arteries, ***Computerized Medical Imaging and Graphics***, Special issue paper, (in press), 2013.

13-5a Deleaval F, Bouvier A, Finet G, Cloutier G, Yazdani SK, Le Floc'h S, Clarysse P, Pettigrew RI, **Ohayon J**. The intravascular ultrasound elasticity-palpography technique revisited: A reliable tool for the *in vivo* detection of vulnerable coronary atherosclerotic plaques. ***Ultrasound in Medicine and Biology***, (in press), 2013.

13-6a Bouvier A, Deleaval F, Doyley MM, Yazdani SK, Finet G, Le Floc'h S, Cloutier G, Pettigrew RI, **Ohayon J**. A Direct Vulnerable Atherosclerotic Plaque Elasticity Reconstruction Method Based on an Original Material-Finite Element Formulation: Theoretical Framework. ***Phys. Med. Biol.***, (in press), 2013.

13-7a Födi E, McAreavey D, Abd-Elmoniem KZ, **Ohayon J**, Saba M, Elagha A, Pettigrew RI, Gharib AM. Pulmonary vein morphology by free-breathing whole heart magnetic resonance imaging at 3T vs breathhold multi-detector computed tomography. ***Journal of Magnetic Resonance Imaging,*** 37(4):846-52, 2013.

12-1a Malve M, Garcia A, **Ohayon J**, Martinez MA. Unsteady blood flow and mass transfer of a human left coronary artery bifurcation: FSI vs CFD. ***International Communications in Heat and Mass Transfert***, 39(6):745-51, 2012.

12-2a. Le Floc'h S, Cloutier G, Saijo Y, Finet G, Yazdani SK, Deleaval F, Rioufol G, Pettigrew RI and **Ohayon J**. A Four-Criterion Selection Procedure for Atherosclerotic Plaque Elasticity Reconstruction based on *in Vivo* Coronary Intravascular Ultrasound Radial Strain Sequences. ***Ultrasound in Medicine and Biology***, 38(12):2084-97, 2012.

12-3a Fleg JL, Stone GW, Fayad ZA, Granada JF, Hatsukami TS, Kolodgie FD, **Ohayon J**, Pettigrew RI, Sabatine MS, Tearney GJ, Waxman S, Domanski MJ, Srinivas PR, Narula J. Detection of high-risk atherosclerotiv plaque: Current status and future directions- Report of the National Heart, Lung, and Blood Institute working group. ***JACC Cardiovasc Imaging,*** 5(9):941-55, 2012

12-4a Gharib AM, Abd-Elmoniem KZ, Ho VB, Födi E, Herzka DA , **Ohayon J**, Stuber M, Pettigrew RI. 350 Micron Spatial Resolution Coronary MRA at 3T: Initial Study in Healthy Subjects and Patients with Coronary Artery Disease. ***Investigative Radiology*** , 47(6):339-45, 2012.

12-5a **Ohayon J**, Mesnier N, Broisat A, Toczek J, Riou L, Tracqui P. Elucidating atherosclertic vulnerable plaque rupture by modeling cross substitution of ApoE-/- mouse and human plaque component stiffnesses. ***Biomechanics and Modeling in Mechanobiology***, 11(6):801-13, 2012.

11-1a. **Ohayon J**, Gharib AM, Garcia A, Heroux J, Yazdani SK, Malvè M, Tracqui P, Martinez MA, Doblare M, Finet G, Pettigrew RI. Is arterial wall-strain stiffening and additional process responsible for atherosclerosis in

coronary bifurcations? *in vivo* Study Based on Dynamic CT and MRI. ***Am J Physiol Heart Circ Physiol***. 301:H1097-106, 2011.

11-2a. Broisat A, Toczek J, Mesnier N, Tracqui P, Ghezzi C, **Ohayon J**, Riou L. Assessing the low levels of mechanical stress in aortic atherosclerosis lesions from ApoE-/-mouse . ***Arterioscler Thromb Vasc Biol.*** 31(5):1007-10 , 2011.

11-3a. Tracqui P, Broisat A, Toczek J, Mesnier N, **Ohayon J**, Riou L. Mapping elasticity moduli of atherosclerotic plaque in situ via atomic force microscopy. ***Journal of structural Biology*** 174(1):115-23, 2011.

10-1a. Peña E, **Ohayon J**, Usson Y, Azancot A, Doblare M. Simulation of the fetal heart performance by finite element methods. ***Rev. Int. Num. Calc. Dis. Ing. 15:185:211***, 2010.

10-2a. Heroux J, Gharib AM, Danthi NS, Cecchini S, **Ohayon J**, Pettigrew RI. High Affinity αvβ3 Integrin Targeted Optical Probe as a New Imaging Biomarker for Early Atherosclerosis: Initial Studies in Watanabe Rabbits. ***Mol Imaging Biol.***, 12(1):2-8, 2010.

10-3a. Peña E, Tracqui P, Azancot A, Doblare M, **Ohayon J**. Unraveling changes in myocardial contractility during human fetal growth: a finite element analysis based on in vivo ultrasound measurements. ***Ann Biomed Eng.***, 38(8):2702-15, 2010.

10-4a. Mesnier N, Tracqui P, **Ohayon J.** An original force-displacement relationship fix spherical inclusions in multilayered viscoelastic finite media. ***Mechanics of Materials***, 42(3):256-265, 2010.

10-5a. Soloperto G, Keenan NG, Sheppard MN, **Ohayon J**, Wood N, Pennell DJ, Mohiaddin RH, Xu XY. A combined imaging, computational and histological analysis of a ruptured carotid plaque. ***Artery Research,*** 4(2):59-65, 2010

10-6a. Le Floc'h S, Cloutier G, Finet G, Tracqui P, Pettigrew RI, **Ohayon J.** On the potential of a new IVUS elasticity modulus imaging approach for detecting vulnerable atherosclerotic coronary plaques: in vitro vessel phantom study. ***Phys. Med. Biol.***, 55:5701-5721, 2010.

10-7a. Finet G., Huo Y, Rioufol G, **Ohayon J**, Guerin P, Kassab GS. Structure-function relation in the coronary artery tree: from fluid dynamics to arterial bifurcations. ***EuroIntervention***, 6:J10-J15, 2010.

09-1a. Bourdarias C, Gerbi S, **Ohayon J.** A pseudo active kinematic constraint for a biological living soft tissue: An effect of the collagen network. ***Mathematical and Computer Modelling***, 49(11-12): 2170-2181, 2009

09-2a. Le Floc'h S, **Ohayon J**, Tracqui P, Finet G, Gharib AM, Maurice R, Cloutier G, Pettigrew RI. Vulnerable Atherosclerotic Plaque Elasticity Reconstruction Based on a Segmentation-Driven Optimization Procedure Using Strain Measurements: Theoretical Framework. ***IEEE Trans Med Imaging***, 28(7):1126-37, 2009.

09-3a. Kamgoué A, **Ohayon J**, Usson Y, Riou L, Tracqui P. Quantification of cardiomyocyte contraction based on image correlation analysis. ***Cytometry A***, 75(4):298-308, 2009.

09-4a. Tracqui P, **Ohayon J**. An integrated formulation of anisotropic force-calcium relations driving spatio-temporal contractions of cardiac myocytes. ***Philos Transact A Math Phys Eng Sci.,*** 367(1908):4887-905, 2009

09-5a. Boudou T, **Ohayon J**, Picart C, Pettigrew RI, Tracqui P. Nonlinear elastic properties of polyacrylamide gels: implications for quantification of cellular forces. ***Biorheology***, 46(3):191-205, 2009.

09-6a. Kotys MS, Herzka DA, Vonken EJ, **Ohayon J**, Heroux J, Gharib AM, Stuber M, Pettigrew RI. Profile order and time-dependent artifacts in contrast-enhanced coronary MR angiography at 3T: origin and prevention. ***Magn Reson Med***., 62(2):292-9, 2009.

08-1a. Tracqui P, **Ohayon J**, Boudou T. Theoretical analysis of the adaptive contractile behaviour of a single cardiomyocyte cultured on elastic substrates with varying stiffness. ***J Theor Biol***., *255(1):92-105. 2008.*

08-2a. Tzvetkova-Chevolleau T, Stéphanou A, Fuard D, **Ohayon J**, Schiavone P, Tracqui P. The motility of normal and cancer cells in response to the combined influence of the substrate rigidity and anisotropic microstructure. ***Biomaterials***, *29(10):1541-51, 2008.*

08-3a. Eskandari H, Salcudean SE, Rohling R, **Ohayon J.** Viscoelastic characterization of soft tissue from dynamic finite element models. ***Physics in Medicine and Biology,*** 53(22):6569-90, 2008.

08-4a. **Ohayon J**, Finet G, Gharib AM, Herzka DA, Tracqui P, Heroux J, Rioufol G, Kotys MS, Elagha A, Pettigrew RI. Necrotic core thickness asnd positive arterial remodeling index: emergent biomechanical factors for evaluating the risk of plaque rupture. ***Am J Physiol Heart Circ Physiol***., 295(2):H717-27, 2008

07-1a. Kamgoue A, Ohayon J, Tracqui P. Estimation of cell Young's modulus of adherent cells probed by optical magnetic tweezers: influence of cell thickness and bead immersion. ***J. Biomech Engin. ASME***, 129(4):523-30, 2007.

07-2a. **Ohayon J**, Dubreuil O, Tracqui P, Le Floc'h S, Rioufol G, Chalabreysse L, Thivolet F, Pettigrew RI, Finet G. Influence of residual stress/strain on the biomechanical stability of vulnerable coronary plaques: potential impact for evaluating the risk of plaque rupture. ***Am J Physiol Heart Circ Physiol***., 293(3):H1987-96, 2007.

07-3a. Tracqui P., **Ohayon J**. Rotational microrheology of multiplayered finite elastic media. ***Journal of Applied Physics,*** *102:171-176, 2007*

06-1a. Boudou T, **Ohayon J**, Arntz Y, Finet G, Picart C, Tracqui P. An extended modeling of the micropipette aspiration experiment for the characterization of the Young's modulus and Poisson's ratio of adherent thin biological samples: Numerical and experimental studies. ***Journal of Biomechanics***, 39:1677-85, 2006.

06-2a. Boudou T., **Ohayon J**., Picart C., Tracqui P. Characterization of the Young's modulus and Poisson's ratio of polyacrylamide gels using micropipette aspiration technique. ***Biorheology***, 43(6) : 721-8, 2006.

05-1a. **Ohayon J**, Tracqui P. An extended method for computing the apparent stiffness of individual cell probed by magnetic twisting cytometry . ***Annals of Biomedical Engineering***, 33(2): 131-141, 2005.

05-2a. Maurice RL, Daronat M, **Ohayon J**, Stoyanova E, Foster FS, Cloutier G. Non-invasive high-frequency vascular ultrasound elastography. ***Physics in Medicine and Biology***, 50: 1611-1628, 2005.

05-3a. Gerard J.M., **Ohayon J**., Luboz V., Perrier P., Payan Y. Non linear elastic properties of the lingual and facial tissues assessed by indentation technique: Application to the biomechanics of speech production. ***Medical Engineering and Physics ,*** 27(10):884-892, 2005.

05-4a. Francius G, Hemmerlé J, **Ohayon J**, Schaaf P, Voegel JC, Picart C, Senger B. Effect of crosslinking on the elasticity of polyelectrolyte multilayer films measured by colloidal probe AFM. ***Microscopy Research and Technique***, 69(2):84-92, 2005.

05-5a. Pustoc'h A, **Ohayon J**, Usson Y, Kamgoue A, Tracqui P. An integrative model of the self-substained oscillating contractions of cardiac myocytes. ***Acta Biotheoretica***, 53(4) : 277-93, 2005.

05-6a. Tracqui P, Namy P and **Ohayon J**, Cellular networks morphogenesis induced by mechanically stressed microenvironments, ***J. Biol. Phys. Chem***. 5:57-69, 2005.

04-1a. Finet G, **Ohayon J**, Rioufol G. Biomechanical Interaction between Blood Pressure, Cap Thickness, and Lipid Core Composition in Vulnerable Coronary Plaque:Impact on Stability or Instability. ***Coronary Artery Disease*** 15:13-20, 2004.

04-2a. Maurice RL, **Ohayon J**, Frétigny Y, Bertrand M, Soulez G, Cloutier G. Non-invasive vascular elastography : theoretical framework. ***IEEE Transaction on Medical Imaging*** , 23 (2):164-180, 2004.

04-3a. Namy P, **Ohayon J**, Tracqui P. Critical conditions for pattern formation and in vitro tubulogenesis driven by cellular traction fields. ***Journal of Theoretical Biology***, 227 (1): 103-120, 2004.

04-4a. Tracqui P, **Ohayon J.** Influence of the cellular nucleus on the cell mechanical response during magnetic bead twisting. ***Acta Biotheoretica****, 52 (4):323-341, 2004.*

04-5a. Maurice RL, **Ohayon J**, Finet G, Cloutier G. A model-baed approach devoted to endovascular elastography. ***J. of the Acoustical Society of America****, 116 (2):1276-1286, 2004.*

04-6a. **Ohayon J**, Tracqui P, Fodil R, Laurent VM, Planus E, Isabey D. Finite Element Analysis of Strain Hardening Properties of Adherent Epithelial Cells Assessed by Magnetic Bead Twisting. ***J. Biomech Engin. ASME***, 126: 685-698, 2004.

03-1a. Bourdarias C, Gerbi S, **Ohayon J**. A three dimensional finite element method for biological active soft tissue -Formulation in cylindrical polar coordinates. ***Mathematical Modelling and Numerical Analysis***. M2AN, 37 (4) :725-739, 2003.

02-1a. **Ohayon J**, Cai H, Jouk PS, Usson Y. and Azancot A. A model of the structural and functional development of the normal human fetal left ventricle based on a global growth law. ***Computer Methods in Biomechanics & Biomedical Engineering.*** 5(2) :113-126, 2002.

01-1a. **Ohayon J**, Teppaz P, Rioufol G. and Finet G., *In vivo* prediction of human coronary plaque rupture location using intravascular ultrasound and finite element method. ***Coronary Artery Disease***. 12 :655-663, 2001.

99-1a. **Ohayon J**, Usson Y, Jouk PS, Cai H. Fiber orientation in human fetal heart and ventricular mechanics: A small perturbation analysis. ***Computer Methods in Biomechanics & Biomedical Engineering*** 2:83-105, 1999.

95-1a. **Ohayon J**, Chadwick RS, Herbin R. Nonuniform cavity pressure and ventricular mechanics. ***Mechanical Research Communication*** *22 (3): 205-219, 1995*

94-1a. Pelle G, **Ohayon J**, Oddou C. Trends in cardiac dynamics : Toward coupled model of intracavity fluid dynamics and deformable wall mechanics. ***Journal of Physics III*** *4: 1121-1127, 1994*

91-1a. Brun P, Malak J, Bui MH, Duval AM, **Ohayon J.** A modelized distribution of a actomyosin interactions in the vertebrate cardiac muscle. ***Biorheolgy*** *28, 143-150, 1991.*

90-1a. Chadwick RS, Tedgui A, Michel JB, **Ohayon J**, Levy BI. Phasic regional myocardial inflow and outflow : comparison of theory and experiments. ***American Journal of Physiology*** *258:H1687-H1698, 1990*

89-1a. Chadwick RS, **Ohayon J**, Lewkowicz M. Wall thickness and midwall radius variations in ventricular mechanics. ***Proc. Natl. Acad. Sci****. 86: 2996-2999, 1989.*

88-1a. **Ohayon J**, Chadwick RS. Theoretical analysis of the effects of a radial activation wave and twisting motion on the mechanics of the left ventricle. ***Biorheology****, 25(3):435-447, 1988.*

88-2a. **Ohayon J**, Chadwick RS. Effects of collagen microstructure on the mechanics of the left ventricle. ***Biophysical Journal*** *54: 1077-1088, 1988.*

84-1a. Pelle G, **Ohayon J**, Oddou C, Brun P. Theoritical models in the left ventricle. ***Biorheology****. 21:709-722, 1984*

Articles Soumis à des Comités de Lecture et Publiés dans des Revues Nationales (n=18)

Peer-Reviewed French National Journal Articles (n=18)

11-1a. Finet G, Rioufol G, **Ohayon J**. La plaque d'athérosclérose coronaire et l'exercice physique. ***AMC Pratique***, 199: 9-14, 2011.

07-1a. Finet G, **Ohayon J**, Rioufol G, Le Floc'h S, Tracqui P, Dubreuil O, Tabib A. Morphological and biomechanical aspects of vulnerable coronary plaque. ***Arch Mal Coeur Vaiss***.,100(6-7):547-53, 2007.

03-1a. Treyve F, **Ohayon J**, Finet G, Rioufol G. Répartition des contraintes au sein d'une plaque d'athérome coronarienne chez l'homme à partir d'un modèle 3D aux éléments finis. ***Comptes Rendus de l'Académie des Sciences , Mécanique*** *331 :449-454, 2003.*

03-2a. Usson Y, Raoult A, **Ohayon J**, Jouk PS. Modélisation géométrique et organisation des fibres myocardiques, Dossier "Le COEUR" ***Pour la Science*** pp : 112-113, Juil/Sept 2003.

00-1a. Finet G, Abrysch F, Rioufol G, **Ohayon J**, Lagache M. Description qualitatives et quantitatives des mécanismes d'action du ballon d'angioplastie sur la sténose coronaire. ***Archives des Maladies du Cœur et des Vaisseaux,*** *93*-9 :1109-1117, 2000.

99-1a. Teppaz P, Finet G, Tabib A, **Ohayon J**. Evaluation des contraintes résiduelles dans les artères coronaires humaine normales. ***I.T.B.M***. 20(1):59-66, 1999.

99-2a. Cai H, Usson, Y, Jouk, PS, **Ohayon, J**. Fiber orientation in mid-trimester human fetal heart and ventricular mechanics. ***I.T.B.M.*** 20(2): 67-83, 1999.

98-1a. Pastor J., **Ohayon, J**., Disdier C. Homogénéisation périodique et composite à fibres actives. ***Comptes Rendus de l'Académie des Sciences*** *, Serie II, 1998.*

97-1a. Teppaz P, **Ohayon J**, Herbin R. Fluid-active structure interaction: Arterial Flow. ***Comptes Rendus de l'Académie des Sciences*** *, Serie II, 324: 37-45, 1997.*

97-2a. **Ohayon J**. An analytical approach to the biomechanics of the intestinal contraction. ***Comptes Rendus de l'Académie des Sciences*** *, Serie II, 324: 179-187, 1997.*

94-1a. **Ohayon J**, Pellissier S, Eribon O, Roche M. Mechanics of the intestinal contraction. ***Comptes Rendus de l'Académie des Sciences*** *, Serie II, 319: 173-180, 1994.*

93-1a. **Ohayon J**, Chadwick RS, Azancot-Benisty A, Ito Y. Distortion of the left ventricle by the right ventricle. ***Comptes Rendus de l'Académie des Science****s , Serie II, 317: 877-884, 1993.*

91-1a. Oddou C., **Ohayon J**, Boulos M. Coeur et mécanique des solides : un bilan positif. ***R.B.M****. N°5, Vol.13:287-290, 1991.*

87-1a. **Ohayon J**, Oddou C. Analyse de la performance cardiaque à partir d'un modèle de ventricule gauche tenant compte de la structure fibreuse du myocarde. ***Journal de Biophysique et Biomécanique*** *11(4):145-154, 1987.*

87-2a. **Ohayon J**, Chadwick RS, Oddou C. Effet d'une excitation intramyocardique radiale et uniforme sur la mécanique du ventricule gauche. Etude théorique. ***Comptes Rendus de l'Académie des Sciences*** *, Serie II, (305): 335-338, 1987.*

86-1a. Rygole AL, **Ohayon J**, Oddou C. Modèles physiques en vue de l'estimation de la performance cardiaque. ***Journal de Biophysique et Biomécanique*** *10(1):31-39,* 1986.

85-1a. Brun P, Pelle G, Vignon P, Estampes B, Malak J, **Ohayon J**, Roulet C. Normalisation des dimensions du ventricule gauche mesurées par échocardiographie. ***Arch . Mal . Coeur*** *78(10):1521-1527, 1985.*

85-2a. **Ohayon J**, Rygole AL, Pelle G, Oddou C. Modèle d'écrasement des petits vaisseaux coronariens dans la paroi du ventricule gauche. ***Journal de Biophysique****, 9 (4):316-317, 1985.*

Articles Soumis à des Comités de Lecture et Publiés dans des Livres (n=21)

Invited Book Chapters (n=21)

06-1b. Tracqui P., Namy P., **Ohayon J**. In vitro tubologenesis of endotheial cells: Analysis of a bifurcation process controlled by a mechanical switch, in Mathematical Modeling of Biological Systems, In: *Mathematical Modeling of Biological Systems, Volume I.* A. Deutsch, L. Brusch, H. Byrne, G. de Vries and H.-P. Herzel (eds). Birkhhauser, Boston, 49-60, 2007.

05-1b. **Ohayon J**., Finet G., Treyve F., Rioufol G., Dubreuil O. A three-dimensional finite element analysis of stress distribution in a coronary atherosclerotic plaque: In-vivo prediction of plaque rupture location. *Biomechanics Applied to Computer Assisted Surgery.* Research Signpost Publisher, Y. Payan editor, 2005.

04-1b. Pustoc'h A., **Ohayon J**., Usson Y., Tracqui P., Modelling the oscillating calcium-induced anisotropic contraction of cardiac myocytes, Dans *" Mecano Transduction, matériaux et structures des sciences de l'ingénieur et du vivant "*, 2004.

04-2b. Gérad J.M., **Ohayon J**., Vincent L., Perrier P., Payan Y. Indentation for estimating the human tongue soft tissues constitutive law: *Application to a 3D biomechanical model. Medical Simulation* – Springer Verlag LNCS 3078, pp. 77-83, 2004.

03-1b. **Ohayon J**., Bourdarias C., Gerbi S. Does the collagen network contributes to normal systolic left ventricular wall thickening ? A theoretical study in continuum mechanics. *FIMH03* – Springer Verlag LNCS 2674, pp. 91-100, 2003.

00.1b. **Ohayon, J**., Cai H., Usson Y., Jouk P.S., Azancot A. Loi de comportement d'un tissu vivant: application à la mécanique de la croissance du coeur foetal humain. Dans *" Mecano Transduction, matériaux et structures des sciences de l'ingénieur et du vivant "*, Ribreau, Berthaud, Moreau et col. Eds. Editions TecLavoisier ,91-97, 2000.

98-1b. Oddou, C., **Ohayon, J**., Mécanique de la structure cardiaque. Biomécanique des Fluides et des Tissus - M.Y. Jaffrin, F. & Goubel F. eds, Masson, 247-292, 1998.

94-1b. Pelle, G.,Tran Van, V., Naili, S., **Ohayon, J**., Oddou, C. Numerical models for the fluid-structure interaction applied to cardiac mechanics *METABIEF* - Springer Verlag ed.

93-1b. Chadwick, R.S., Azancot-Benisty, A., **Ohayon, J**., Ito Y. Right and left ventricle interaction and remodeling in congenital heart disease. Interactive Phenomena in the Cardiac System- Sideman, S. and Beyard, R. eds, Plenum Press, 373-381,1993

91-1b. Chadwick, R.S., Lewkowicz, M., **Ohayon, J**. An analytical approach to the biomechanics of some cardiac diseases. *Imaging, Measurements and Analysis of the Heart* - Sideman, S. and Beyard, R. eds. Hemisphere Publishing Cooporation, Washington D.C., 99-112, 1991.

91-2b. Oddou, C., Boulos, M., **Ohayon, J**., Crozatier, B. Numerical model of fibrous and ovoid structure: Application to the cardiac system. *Computer in Biomedicine* - K.D. Held, C.A. Brebbia and R.D. Ciskowski eds.Computational Mechanics Publications, Southampton, 13-21, 1991.

88-1b. **Ohayon, J**. Evolution of models of the mechanics of the left ventricle. *Cardiovascular Dynamics and Models.* Brun, P., Chadwick, R.S., and Levy, B., eds. Edition INSERM Vol 183, 104-111, Paris, 1988.

88-2b. Oddou, C., **Ohayon, J**., Samake, J. Intramyocardial blood vessel lumen deformation. *Cardiovascular Dynamics and Models*. Brun, P., Chadwick, R.S., and Levy, B., eds. Edition INSERM Vol 183, 38-43, Paris, 1988.

88- 3b. Vignon, P., Pelle, G., **Ohayon, J**., Brun, P. Instantaneous systolic relationship between the left ventricle wall thickness and cavity radius by echocardiography. *Cardiovascular Dynamics and Models.* Brun, P., Chadwick, R.S., and Levy, B., eds. Edition INSERM Vol 183, 264-275, Paris, 1988.

88-4b. **Ohayon, J**., Chadwick, R.S. Collagen in the myocardium and its influence on the mechanics of the left ventricle. *Cardiovascular Dynamics and Models.* Brun, P., Chadwick, R.S., and Levy, B., eds. Edition INSERM Vol 183, 168-181, Paris, 1988.

88-5b. **Ohayon, J**., Chadwick, R.S. Mechanics of the left ventricle: effects of a radial activation wave and twisting motion. *Cardiovascular Dynamics and Models.* Brun, P., Chadwick, R.S., and Levy, B., eds. Edition INSERM Vol 183, 146-150, Paris, 1988.

88-6b. Chadwick, R.S., **Ohayon, J**. Axisymmetric geometrical effects in ventricular mechanics *Cardiovascular Dynamics and Models.* Brun, P., Chadwick, R.S., and Levy, B., eds. Edition INSERM Vol 183, 193-202, Paris, 1988.

88-7b. Chadwick, R.S., **Ohayon, J**. A theory for local energetics and oxygen demand based on an active rheological law. *Cardiovascular Dynamics and Models.* Brun, P., Chadwick, R.S., and Levy, B., eds. Edition INSERM Vol 183, 151-159, Paris, 1988.

88-8b. Chadwick, R.S., Tedgui, A., Michel, J.B., **Ohayon, J**. , Levy, B. A theoretical model for phasic regional myocardial inflow and outflow : comparison with experiments. *Cardiovascular Dynamics and Models.* Brun, P., Chadwick, R.S., and Levy, B., eds. Edition INSERM Vol 183, 77-90, Paris, 1988.

88-9b. Brun, P., **Ohayon, J**., Bui, M.H., Malak, J., Pelle, G. Simulation of myocardial dynamics at an elementary level: I Dynamic distribution of actomyosin interactions in vertebrate cardiac muscle. *Cardiovascular Dynamics and Models.* Brun, P., Chadwick, R.S., and Levy, B., eds. Edition INSERM Vol 183, 203-213, Paris, 1988.

88-10b. Brun, P., Malak, J., **Ohayon, J**., Pelle, G., Vignon, P. Simulation of myocardial dynamics at an elementary level: II Simulation of myocardial sarcomere and fiber mechanics. *Cardiovascular Dynamics and Models.* Brun, P., Chadwick, R.S., and Levy, B., eds. Edition INSERM Vol 183, 214-221, Paris, 1988.

Congrès Internationaux avec Actes (n=60)

International Conferences with Proceedings or Extended Abstracts (n=60)

14-1c. **Ohayon J**, Riou L, Finet G, Pettigrew RI. Atherosclerotic plaque rupture: mouse versus man **World Congress of Biomechanics**, WCB 2014, Boston, MA, USA, 6-11July 2014.

14-2c. **Ohayon J**, Le Floc'h S, Bouvier A, Finet G, Cloutier G, Pettigrew RI. Elasticity reconstruction methods for atherosclerotic plaque detection and characterization. **World Congress of Biomechanics**, WCB 2014, Boston, MA, USA, 6-11July 2014.

14-3c. Yazdani SK, Parks A, Kim SH, Atigh M, Pettigrew RI, **Ohayon J**. An enothelialized coronary bifurcation model. **World Congress of Biomechanics**, WCB 2014, Boston, MA, USA, 6-11July 2014.

13-1c. **Ohayon J**, Deleaval F, Bouvier A, Le Floc'h S, Finet G, Cloutier G, Pettigrew RI. The elasticity-palpography technique revisited: Detection of atherosclerotic plaques. **Congress of the European Society of Biomechanics**, ESB 2013, Patrace, Greece, 25-28 August 2013.

13-2c. **Ohayon J**, Deleaval F, Bouvier A, Le Floc'h S, Finet G, Cloutier G, Pettigrew RI. The improved elasticity-palpography technique: In vivo detection of vulnerable atherosclerotic plaques. **International Conference on Computational Bioengineering**, ICCC 2013, Leuven, Belgium, 11-13 September 2013.

13-3c. Keshavarz-Motamed Z, Le Floc'h S, Ohayon J, Cloutier G. Improvement of an intravascular ultrasound elasticity modulus imaging approach for detecting vulnerable atherosclerotic plaques. ICA meeting Montreal, Canada, J. Acoust. Soc. Am. 133(5):3541, 2-7 June 2013.

13-4c. Cloutier G, Majdouline Y, Garcia D, Allard L, Lerouge S, **Ohayon J**, Soulez G. Radial shear strain elastography imaging of carotid atherosclerotic plaques in a porcine model. ICA Montreal, Canada, J. Acoust. Soc. Am. 133(5):3540, 2-7 June 2013.

12-1c. S. Le Floc'h, G. Cloutier, Y. Saijo, G. Finet, P. Tracqui, R.I. Pettigrew, **J. Ohayon**. New criteria to extract reliable atherosclerotic plaque modulograms from in vivo coronary IVUS strain sequence. **Euromech 534 - Colloquium on advanced experimental approaches and inverse problems in tissue biomechanics**, May 28-31, 2012, Saint-Etienne, France.

12-2c. C Schmitt, A Hadj Henni, S LeFloc'h, J **Ohayon**, J Vappou, G Cloutier. Hyper-frequency viscoelastic spectroscopy of a mimicking vascular phantom and porcine aorta with the rhoespectris instrument. **International Tissue Elasticity Conference** (ITEC) 2012. Deauville, France, 2-5 October 2012.

12-3c. **Ohayon J**, Deleaval F, Le Floc'h S, Bouvier A, Finet G, Cloutier G. The Intravascular Ultrasonic Palpography Technique Revisited: Vulnerable Atherosclerotic Plaque Elasticity Reconstruction. **8th International Conference on Ultrasonic Biomedical Microscanning**. Canada-Quebéc, September 24-27, 2012

12-4c. Deleaval F, Le Floc'h S, Bouvier A, Finet G, Clarysse P, **Ohayon J**. Viscoelastic Characterization of Vulnerable Atherosclerotic Plaques based on Coronary Intravascular Ultrasound Radial Strain Sequences. **8th International Conference on Ultrasonic Biomedical Microscanning**. Canada-Quebéc, September 24-27, 2012

12-5c. **Ohayon J**, Broissat A, Riou L, Tracqui P. Stability of vulnerable plaques in humans and ApoE mice. **Congress of the European Society of Biomechanics**, ESB 2012 Lisbon, Portugal, July 1-4, 2012.

12-6c. Le Floc'h S, Cloutier G, Finet G, Tracqui P, Pettigrew RI, **Ohayon J**. Performance of a new elasticity modality used for the detection of atherosclerotic plaques. **Congress of the European Society of Biomechanics**, ESB 2012 Lisbon, Portugal, 1-4 July 2012.

12-7c. **Ohayon J**, Le Floc'h S, Saijo Y, Finet G, Cloutier G, Pettigrew RI. A new intravascular ultrasound imaging technique for coronary atherosclerotic plaques detection and rupture prediction. **7th International symposium on Biomechanics in Vascular Biology and Cardiovascular Disease**. Atlanta, USA, 25-27th April 2012.

12-8c. Majdouline Y, **Ohayon J**, Garcia D, Roy Cardinal MH, Soulez G, Cloutier G. Shear strain endovascular elastography for characterizing atherosclerotic plaques: A validation study *in vivo*. **7th International symposium on Biomechanics in Vascular Biology and Cardiovascular Disease**. Atlanta, USA, 25-27th April 2012.

12-9c. Gharib AM, Abd-Elmoniem KZ, Ho VB, Födi E, Herzka DA , **Ohayon J**, Stuber M, Pettigrew RI. The Feasibility of 350 Micron Spatial Resolution Coronary MRA at 3T in Humans. **SCMR** 15th Annual Scientific Sessions meeting, February 2-5, 2012 at the Marriott World Center in Orlando, FL, USA

11-1c. Tracqui P, Broisat A, Toczek J, Mesnier N, Riou L., **Ohayon J**. Mechanical characterization of atherosclerotic plaque components using atomic force microscopy. **6th International symposium on Biomechanics in Vascular Biology and Cardiovascular Disease**. Rotterdam, the Netherlands, 14-15 April 2011.

11-2c. Broisat A, Toczek J, Mesnier N, Tracqui P, Ghezzi C, Riou L., **Ohayon J**. Low levels of mechanical stress in aortic atherosclerotic lesions from ApoE-/- mouse: Potential implications for plaque stability. **6th International symposium on Biomechanics in Vascular Biology and Cardiovascular Disease**. Rotterdam, the Netherlands, 14-15 April 2011.

11-3c. Y. Majdouline, S. Le Floc'h, D. Garcia, M.H. Roy Cardinal, **J. Ohayon**, G. Cloutier. Shear strain endovascular elastograpy : Validation with in vitro data. **10th International Tissue Elasticity Conference** (ITEC) 2011. Arlington, Texas, USA, 10-15 October 2011.

11-4c. G. Cloutier, S. Le Floc'h, Y. Saijo, G. Finet, P. Tracqui, R.I. Pettigrew, **J. Ohayon**. Performance of new mechanical criteria used to extract in vivo valid modulograms from a cardiac cycle coronary IVUS strain sequence. **10th International Tissue Elasticity Conference** (ITEC) 2011. Arlington, Texas, USA, 10-15 October 2011.

11-5c. E. Mercure, F. Destrempes, Y. Majdouline, **J. Ohayon**, G. Soulez, G. Cloutier. Reducing artifacts in non-invasive vascular elastography of carotid arteries. **10th International Tissue Elasticity Conference** (ITEC) 2011. Arlington, Texas, USA, 10-15 October 2011.

11-6c. Y. Majdouline, D. Garcia, S. Le Floc'h, M.H. Roy Cardinal, F. Destrempes, **J. Ohayon**, G. Cloutier. Shear strain endovascular elastograpy for characterizing atherosclerotic plaques: In vitro vessel phantom study. **14th International Conference on Medical Image Computing and Computer Assisted Intervention** (MICCAI) 2011. Toronto, Canada, 18-22 September 2011.

11-7c. E. Mercure, F. Destrempes, **J. Ohayon**, G. Soulez, G. Cloutier. Quantitative parameter extraction from axial strain maps in non-invasive vascular elastography of carotid arteries. **14th International Conference on Medical Image Computing and Computer Assisted Intervention** (MICCAI) 2011. Toronto, Canada, 18-22 September 2011.

11-8c. Malvè M, Gharib AM, Yazdani SK, Martinez MA, Finet G, Doblare M, Virmani R, Pettigrew RI**, Ohayon J**,. Tortuosity of coronary arteries as a potential local risk factor for atherosclerosis. **Euromech 529 – Cardiovascular Fluid Mechanics** CVFM2011, University of Cagliari, Italy, 27-29 June 2011.

11-9c. Finet G., **Ohayon J**, Rioufol G. New insight in coronary vulnerable plaque mechanical properties. **11th ARTERY** 2011. Paris, France, 13-15 October 2011.

10-1c. Cloutier G, Le Floc'h S, Saijo Y, Gharib AM, Finet G, Pettigrew RI, **Ohayon J.** Intravascular ultrasound elastography and modulography of coronary atherosclerotic plaques for rupture prediction. **International Symposium on Biomedical Simulation** ISBMS 2010 – Phoenix, Arizona, USA, 23-24 Janvier 2010.

10-2c. Majdouline Y., Saijo Y., Destrempes F., **Ohayon J.**, Cloutier G., Intravascular ultrasound elastography of coronary arteries: A pre- and post-atherectomy study, **9th Int. Conf. Meas. Imag. Tissue Elasticity**, Snowbird, Utah, USA, 2010.

10-3c. Le Floc'h S, Finet G, Tracqui P, Cloutier G, Pettigrew RI, **Ohayon J**. Young's modulus reconstruction of coronary vulnerable plaque based on a segmentation-driven optimization procedure: Influence of the intrinsic compressibility of the medium. **Congress of the European Society of Biomechanics**, ESB 2010 Edinburgh, UK, 5-8 July 2010.

10-4c. Tracqui P, **Ohayon J**, Vaihé B. Mechanobiology of angiogenesis: analysis of feedback loops between cellular stress and extracellular matrix proteolysis. **Congress of the European Society of Biomechanics**, ESB 2010 Edinburgh, UK, 5-8 July 2010

10-5c. **Ohayon J**, Gharib AM, Garcia A, Finet G, Martinez MA, Pettigrew RI. Endothelial strain distribution in human left main coronary bifurcation. **Congress of the European Society of Biomechanics** ESB 2010, Edinburgh, UK, 5-8 July 2010.

10-6c. Le Floc'h S, Finet G, Tracqui P, Cloutier G, Pettigrew RI, **Ohayon J**. IVUS modulography of coronary plaques based on a segmentation-driven optimization procedure: theoretical Frameworks. **IV European Conference on Computational Mechanics** ECCM 2010 – Paris, France, May 16-21, 2010.

10-7c. Tracqui P, **Ohayon J**. Toward a multi-scale modelling of cardiac tissue self-adaptive contractility. **IV European Conference on Computational Mechanics** ECCM 2010 – Paris, France, May 16-21, 2010.

09-1c. **Ohayon J**, Finet G, Gharib AM, Pettigrew RI. Emergent morphological factors for evaluating the risk of coronary plaque rupture. **4th International symposium on Biomechanics in Vascular Biology and Cardiovascular Disease.** Rotterdam, the Netherlands, 16-17th April 2009.

09-2c. Le Floc'h S, **Ohayon J**, Tracqui P, Finet G, Gharib A, Maurice R, Cloutier G, Pettigrew R. Modulography of vulnerable atherosclerotic plaques based on a segmentation-driven optimization procedure using strain measurements. **4th International symposium on Biomechanics in Vascular Biology and Cardiovascular Disease.** Rotterdam, the Netherlands, 16-17th April 2009.

08-1c. Herzka, DA, Kotys, MS, Krueger S, Traughber BJ, Heroux, J, Gharib, AM, **Ohayon, J**, Weiss S, Pettigrew, RI, Wood, BJ. MR-guided catheter-based excitation emission optical spectroscopy for in vivo tissue characterization. **Society of Photo-Optical instrumentation engineers**, 6918:U9181, 2008.

07-1c. Boudou T, **Ohayon J**, Picart C, Tracqui P. Influences of adhesion area and biological sample size on the estimation of Young's modulus and Poisson's ratio assessed by micropipette aspiration technique. **Conf Proc IEEE Eng Med Biol** Soc., 5391-4, 2007

06-1c. Pena E., Doblaré M., Azancot A., **Ohayon J**. Finite element study of beating fetal heart. **International Symposium on Computer Methods in Biomechanics & Biomedical Engineering**, 22-25 Mars 2006, Juan les Pins, France.

06-2c. Goicolea J.M., **Ohayon J**., Pelletier A., Sanz B. Visco-hyperelastic models for mechanical studies of atherosclerotic vessels. **European Conference on Computational Mechanics**, Lisbon, 5-8 june 2006, Portugal.

06-3c. Tracqui P., **Ohayon J.** Active and Passive mechanical behavior of a cardiac cell driven by oscillatory calcium dynamics. **5th World Congress of Biomechanics**. Munich, Germany, 1-4 August 2006

06-4c. **Ohayon J.**, Finet G., Dubreuil O., Rioufol G., Le Floc'h S., Tracqui P. Influence of residual stress on local stress distribution in the human atherosclerotic coronary artery. **5th World Congress of Biomechanics**. Munich, Germany, 1-4 August 2006.

06-5c. Tracqui P., **Ohayon J.** Modeling and simulation of cardiac tissue deformations. **2nd workshop on Computer Assisted Diagnostic and Surgery**, Chili, March 2006.

04-1c. Pustoc'h A., **Ohayon J**., Boudou T., Usson Y., Tracqui P., A mechano-chemical model of the calcium-induced cardiomyocyte contraction, **WSEAS**, July 2004, Greece.

04-2c. Boudou T., Tracqui P., Finet G., **Ohayon J**., A finite element approach for Analysis of the Micropipette Experiment for Thin Biological Samples, **WSEAS**, July 2004, Greece.

03-1c. Maurice R.L., **Ohayon J**., Finet G., Soulez G., Cloutier G. Non-invasive vascular elastography : Theoretical Investigation. **2nd International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity**. USA, 2003.

02-1c. Bourdarias C., Gerbi S., **Ohayon J**. A finite element method for the contraction analysis of cardiac tissue under pseudo-active kinematic constraint. **9th FEM Workshop**, July 18th and 19th 2002.

02-2c. Maurice R.L., Frétigny Y., **Ohayon J.**, Bertrand M., Soulez G., Cloutier G. Non-invasive vascular elastography : a prospective study. **IEEE International Ultrasonics Symposium**, Munich, Germany, October 2002.

01-1c. Bourdarias C., Gerbi S., **Ohayon, J**. A finite element method for an active soft tissue. **1st SIAM-EMS Conference**, 2-6 september 2001, Berlin, Germany.

01-2c. **Ohayon J.**, Teppaz P., Rioufol G., Finet G. In vivo prediction of human coronary plaque rupture location : Computational structural analysis based on intravascular ultrasound imaging. **International Symposium on Computer Methods in Biomechanics & Biomedical Engineering**, 31th October- 4 November, 2001, Rome, Italy.

01-3c. Finet G., Rioufol G., **Ohayon J**. Impact of biomechanical factors on prediction of coronary atherosclerotic plaque fracture location : Computational structural analysis based on intravascular ultrasound imaging. **International Symposium on Computer Methods in Biomechanics & Biomedical Engineering**, 31th October- 4 November, 2001, Rome, Italy.

01-4c. **Ohayon J.**, Bourdarias C., Gerbi S., Oddou C. A finite element method for the active cardiac muscle. **International Symposium on Computer Methods in Biomechanics & Biomedical Engineering**, 31th October- 4 November, 2001, Rome, Italy.

01-5c. **Ohayon J.**, Usson Y., Jouk P.S., Azancot A. Structural and functional development of the normal human fetal left ventricle : Inference in the performance analysis of hypoplastic right ventricular hearts. **International Symposium on Computer Methods in Biomechanics & Biomedical Engineering**, 31th October- 4 November, 2001, Rome, Italy.

92-1c. Pelle, G., **Ohayon, J.**, Oddou, C. Trends in cardiac dynamics : Toward coupled model of intracavity fluid dynamics and deformable wall mechanics. **ICFM4** , 28-30 avril 1992, Alexandrie, Egypte.

88-1c. Chadwick, R.S., **Ohayon, J**. Strain energy stored in the myocardium at end-systole as a filling index of the heart. **Society of Engineering Science Meeting**, Univ of California at Berkeley, June 20-22,1988.

88-2c. Chadwick, R.S.,**Ohayon, J**. Mechanics of the arteriole wall. **World Congress on Medical Physics and Biomedical Engineering**; (33)1:349, San Antonio, Texas, august 9-12, 1988.

88-3c. **Ohayon, J**., Lewkowicz, M., Chadwick, R.S. Fluid-Fiber-Collagen description of the myocardium applied to different left ventricular geometries. **World Congress on Medical Physics and Biomedical Engineering**; (33)1:179, San Antonio, Texas, august 9-12, 1988.

87-1c. **Ohayon, J**., Chadwick, R.S. Effect of Collagen on the Elasticity of the Myocardium **8th International Conference of the Cardiovascular System Dynamics Society**, Japan 1987.

87-2c. **Ohayon, J**., Chadwick, R.S. Mechanics of the left ventricle : Effects of radial activation and twisting motion. Proceedings of **13th Northeast Bioengineering Conference**, University of Pennsylvania, Phil.,U.S.A, March 12-13, 1987.

87-3c. Chadwick, R.S., **Ohayon, J**. A theory for regional myocardial blood flow. Proceedings of **13th Northeast Bioengineering Conference**, University of Pennsylvania, Phil., U.S.A , March 12-13, 1987.

86-1c. Chadwick, R.S., **Ohayon, J**. A theory for regional myocardial blood flow. **ASME Annual meeting**, Annaheim CA, U.S.A, December 7-12, 1986. Published in ASME 1986 Advances in Bioengineering.

85-1c. Oddou, C., **Ohayon, J**., Rygole, A.L., Pelle, G. The collapse of small coronary vessel in the myocardium. **XIV ICMBE and VIIICMP**; 1319-1320, Espoo, Finland, August 11-16, 1985.

84-1c. Oddou, C., **Ohayon, J**., Pelle, G.,Brun, P. Quasi-static analysis of the left ventricle dynamics. **4th International conference on Mechanics in Medicine and Biology**; 203-206, Buffalo, july 8-11, 1984.

Congrès Nationaux avec Actes (n=36)

French National Conferences with Proceedings or Extended Abstracts (n=36)

12-1c Deleaval F, Le Floc'h S, Bouvier A, Finet G, Cloutier G, **Ohayon J**. Ultrasonic Assessment of Arterial Wall Elasticity: The Palpography Technique Revisited. ***Comput Methods Biomech Biomed Engin.*** 2012 Sep;15 Suppl 1:36-7.

11-1c. Le Floc'h S, Finet G, Saijo G, Tracqui P, Pettigrew RI, Cloutier G, **Ohayon J.** From elasticity imaging to peak cap stress estimation in atherosclerotic coronary plaques. Printemps de la Cardiologie, 12-14 May 2011, Lyon, France.

10-1c. **Ohayon J**, Gharib AM, Garcia A, Finet G, Martinez MA, Pettigrew RI. Biomechanics of the atheroma plaque: Identification of high risk zones for atherosclerosis. 4th thematic day of the French Biomechanics Society, "Interdisciplinary forum: How (can) biomedical engineering contribute to understanding, diagnosis and treatment of cardiovascular disease?" Paris, France, 16-17 December 2010.

10-2c. Mesnier N, Broissat N, Toczek J, Riou L, Fagret D, Tracqui P, **Ohayon J**. Intraplaque residual stress/strain distributions and biomechanical stability of mouse atherosclerotic aortic plaque. 35ème Congrès de la Société de Biomécanique, 25-27 Aout 2010, Nantes, France.

10-3c. Le Floc'h S, Finet G, Tracqui P, Pettigrew RI, Cloutier G, **Ohayon J**. Imaging modulography of coronary plaques : An experimental in vitro study. 35ème Congrès de la Société de Biomécanique, 25-27 Aout 2010, Nantes, France.

10-4c. Le Floc'h S, Finet G, Saijo Y, Tracqui P, Pettigrew RI, Cloutier G, **Ohayon J.** Elasticity imaging of vulnerable atherosclerotic coronary plaques. Congrès de la Société Française de Cardiologie, 15-17 Avril 2010, Nantes, France.

07-1c. Boudou T., **Ohayon J**., Picart C., Tracqui P. Caractérisation des propriétés mécaniques des gels de polyacrylamide à l'aide de la technique d'aspiration par micropipette. 18ème Congrès Français de Mécanique, 27-31 Août 2007, Grenoble, France.

07-2c. Le Floc'h S., **Ohayon J**., Tracqui P., Finet G. Caractérisation des propriétés anisotropes de la plaque d'athérome coronarienne. 18ème Congrès Français de Mécanique, 27-31 Août 2007, Grenoble, France.

07-3c. Kamgoue A., **Ohayon J**., Tracqui P. Caractérisation des propriétés mécaniques de cellules endothéliales à l'aide de la technique de pinces optiques. 18ème Congrès Français de Mécanique, 27-31 Août 2007, Grenoble, France.

04-1c. Boudou T., Tracqui P., Finet G., **Ohayon J**., Analysis of the Micropipette Experiment for Thin Biological Samples, XXIXème Congrès de la Société de Biomécanique, Septembre 2004, Créteil, France.

03-1c. Tracqui P., **Ohayon, J**., Fodil R., Planus E., Laurent V., Isabey D. Propriétés hyperélastiques de la cellule épithéliale : étude quantitative réalisée par un modèle aux éléments finis. 16ème Congrès Français de Mécanique, 1-5 Septembre 2003, Nice, France.

03-2c. Treyve F., **Ohayon J**., Finet G., Rioufol G. Répartition des contraintes au sein d'une plaque d'athérome coronarienne chez l'homme : étude comparative entre les modèles aux éléments finis 2D et 3D. 16ème Congrès Français de Mécanique, 1-5 Septembre 2003, Nice, France.

03-3c. **Ohayon, J**., Bourdarias C., Gerbi S. Loi de comportement du tissu myocardique tenant compte d'une contrainte cinématique induite par la matrice de collagène. 16ème Congrès Français de Mécanique, 1-5 Septembre 2003, Nice, France.

03-4c. Tracqui P., **Ohayon, J**., Fodil R., Planus E., Laurent V., Isabey D. Strain hardening response of adherent epithelial cells micromanipulated by magnetic bead twisting. XXVIIIème Congrès de la Société de Biomécanique, 11-12 Septembre 2003, Poitiers, France.

03-5c. **Ohayon, J**., Finet G., Rioufol G.. Biomechanical interactions in vulnerable coronary plaque. XXVIIIème Congrès de la Société de Biomécanique, 11-12 Septembre 2003, Poitiers, France.

02-1c. Bourdarias C., Gerbi S., **Ohayon J**. A finite element method for a biological active soft tissue. MS4CMS'02 – INRIA Rocquencourt. 12-15 novembre 2002.

99-1c. Finet, G., Teppaz P, Rioufol G., Lagache M., Tabib A., **Ohayon, J**. Angioplasty: plaque rupture in human coronaries. XXIVème Congrès de la Société de Biomécanique, 15-17 Septembre 1999, Beaune, France.

99-2c. **Ohayon, J**., Cai, H., Jouk, P.S., Usson, Y., Azancot, A. A model for the growth of the human fetal left ventricle. XXIVème Congrès de la Société de Biomécanique, 15-17 Septembre 1999, Beaune, France.

99-3c. **Ohayon, J**., Cai H., Teppaz, P., Oddou. C. Le muscle cardiaque: un matériau composite hyperélastique à fibres actives. 34ème colloque annuel du Groupe Français de Rhéologie (GFR)-Rhéologie des matériaux du vivant, 18-20 Octobre 1999, Paris, France.

98-1c. Cai, H., Azancot, B., **Ohayon, J**. Modélisation de la croissance du ventricule gauche chez le foetus humain. XXIIIème Congrès de la Société de Biomécanique, 17-18 Septembre 1998, Lyon, France.

98-2c. Teppaz, P., Finet, G., Tabib, A., **Ohayon, J**. Contraintes résiduelles dans les artères coronaires humaines normales. XXIIIème Congrès de la Société de Biomécanique, 17-18 Septembre 1998, Lyon, France.

98-3c. Lagache, M., Finet, G., **Ohayon, J**., Rioufol, G. Distribution des contraintes dans un vaisseau coronarien humain avec plaque d'athérosclérose. XXIIIème Congrès de la Société de Biomécanique, 17-18 Septembre 1998, Lyon, France.

98-4c. Disdier, C., Pastor, J., **Ohayon, J**. Homogénéisation périodique: application au muscle cardiaque. XXIIIème Congrès de la Société de Biomécanique, 17-18 Septembre 1998, Lyon, France.

97-1c. Teppaz, P., **Ohayon, J**., Herbin, R. Mécanique de l'écoulement artériel et lois d'autorégulation 13ème Congrès Français de Mécanique, 1-5 Septembre 1997, Poitiers, France.

97-2c. Cai, H., **Ohayon, J**., Azancot, A. Un modèle mathématique sur la croissance du coeur intégrant l'anisotropie du muscle. 13ème Congrès Français de Mécanique, 1-5 Septembre 1997, Poitiers, France.

97-3c. Pastor, J., **Ohayon, J**. Simulation par homogénéisation périodique du composite musculaire fibreux en état d'activation. 13ème Congrès Français de Mécanique, 1-5 Septembre 1997, Poitiers, France.

95-1c. **Ohayon, J**., Chadwick, R.S., Herbin, R. Comportement mécanique du ventricule gauche sous pression cavitaire non uniforme. 12ème Congrès Français de Mécanique de l'AUM, 4-8 Septembre 1995, Strasbourg, France.

95-2c. Rouffiac, V., Pelle G., **Ohayon, J**., Effet de l'inertie et de viscoélasticité sur le comportement mécanique du ventricule gauche : un modèle 2D. XXème Congrès de la Société de Biomécanique, 11-12 Septembre 1995, Lausanne, Suisse.

95-3c. Teppaz, P., Herbin, R., **Ohayon, J**. Schéma de volumes finis en interaction fluide-structure : faisabilité et application à l'écoulement vasculaire. XXème Congrès de la Société de Biomécanique, 11-12 Septembre 1995, Lausanne, Suisse.

95-4c. Lancry, F., **Ohayon, J**. , Pellissier, S., Roche, M. Mécanique de la contraction intestinale : réponse à une controverse. XXème Congrès de la Société de Biomécanique, 11-12 Septembre 1995, Lausanne, Suisse.

91-1c. **Ohayon, J**., Chadwick, R.S., Azancot-Benisty, A. Influence du ventricule droit sur la mécanique du ventricule gauche 10ème Congrès de l'A.U.M.,Tome 4:29-32, 2-6 septembre 1991, Jussieu, Paris.

88-1c. **Ohayon, J**., Du Burck, F., Djerad, S., Chadwick, R.S., Oddou, C. Analyse des propriétés rhéologiques du tissu myocardique à l'état passif. 13 ème Congrès Annuel de la Société de Biomécanique, Bruxelles, sept 1988.

87-1c. **Ohayon, J**., Chadwick, R.S., Oddou, C. Collagène dans le myocarde et son influence sur la mécanique du ventricule gauche.12 ème Congrès Annuel de la Société de Biomécanique, Paris - C.H.U Necker, 3-4 sept 1987

85-1c. Rygole, A.L., **Ohayon, J**., Oddou, C. Modélisation biomécanique cardiaque : approche du comportement ventriculaire par une cavité cylindrique en matériau composite fibreux. 7ème AUM, 1:174-175, Bordeaux, 1985.

84-1c. **Ohayon, J**., Pelle, G., Rygole, A.L., Oddou, C. Rhéologie de la Fibre Myocardique et Comportement Dynamique du Coeur. 9ème Congrès de la Société de Biomécanique, Toulouse 4-5-6 juillet 1984.

83-1c. **Ohayon, J**., Gomis, A., Pelle, G., Oddou, C., Brun, P. Modélisation du Ventricule Gauche compte tenu de la Structure Fibreuse du Myocarde. 8ème congrès de la Société de Biomécanique, Lyon 7-8 juillet 1983.

83-2c. Gomis, A., Ribreau, C., **Ohayon, J**., Oddou, C. Approche de la Mécanique Ventriculaire Gauche par l'Etude du Comportement d'un Ballonnet Sphérique. 8ème Congrès de la Société de Biomécanique, Lyon 7-8 juillet 1983.

Congrès Internationaux avec Résumés (n=24)

***International Conferences with Abstracts* (n=24)**

12-1d. Deleaval F, Finet G, Rioufol G, Lagache M, Saffre P, **Ohayon J**. Does Malapposed Stents Increase the Coronary Thrombogenecity? International Workshop on Endocoronary Biomechanics and Restenosis, Marseille, May 3-4, 2012.

08-1d. **Ohayon J**., Finet G. Morphological factors and coronary plaque vulnerability International Workshop on Endocoronary Biomechanics and Restenosis. Marseille, June 1-2, 2008, France.

06-1d. **Ohayon J**., Finet G., Dubreuil O., Rioufol G. Coronary plaque rupture and residual stress. International Workshop on Endocoronary Biomechanics and Restenosis. Marseille, June 1-2, 2006, France.

05-1d. Tracqui P., **Ohayon, J**., Planus E. Modelling the heterogeneous spatial transmission of intracellular stress to focal adhesions of adherent cells probed by magnetic twisting cytometry. European conference for mathematical and theoretical biology. Dresden, Germany, July 18-22, 2005.

05-2d. Tracqui P., Namy P., **Ohayon, J**. In vitro tubulogenesis of endothelial cells: theoretical analysis of a mechanical switch by balance between cellular tension and matrix proteolysis. European conference for mathematical and theoretical biology. Dresden, Germany, July 18-22, 2005.

03-1d. Finet, G., **Ohayon, J**., Rioufol G. Biomechanical interaction between blood pressure, cap thickness and lipid core composition in vulnerable coronary plaque. International Workshop on Endocoronary Biomechanics and Restenosis. Paris, march 27-28, 2003, France.

01-1d. Tracqui, P, **Ohayon, J**. Non linear viscoelastic behavior of strained fibrin gels : rheological models and implications for cell traction forces quantification. Israelian-French Satellite Workshop : Tissue & cell engineering from basic research to clinical applications. 23-24 avril 2001, Faculté de médecine de Nancy, France.

00-1d. Lagache, M., Finet, G., Teppaz, P., **Ohayon, J**. Plaque rupture during human coronary angioplasty. International Workshop on Endocoronary Biomechanics and Restenosis. Marseille, april 7, 2000, France.

99-1d. Finet, G., **Ohayon, J**. Biomecanique de la plaque d'atherosclerose. International Workshop on Endocoronary Biomechanics and Restenosis. Marseille, april 9, 1999, France.

98-1d. Azancot, A., **Ohayon, J**., Cai, H. Model for stress induced growth in human fetal heart. XXIII meeting of Association of European Paediatric Cardiologists- Dublin, Ireland, 10-13 june 1998.

98-2d. Cai, H., **Ohayon, J**., Azancot, A., Oddou, C. An anisotropic model for stress induced growth in human fetal heart.Third World Congress of Biomechanics - WCB'98 - Hokkaido University, Sapporo, Japan - August 2-8, 1998.

98-3d. Lagache, M., Finet, G., **Ohayon, J**., Rioufol, G., Oddou, C. In vivo determination of passive unloaded configuration for normal and atherosclerotic arteries bases on intracoronary ultrasound. Third World Congress of Biomechanics - WCB'98 - Hokkaido University, Sapporo, Japan - August 2-8, 1998.

97-1d. Teppaz, P., **Ohayon, J**., Herbin, R. Fluid-active structure interaction in arterial flow. 18th World Congress on Medical Physics ad Biomedical Engineering, September 14-19, 1997, Nice, France.

97-2d. **Ohayon, J**., Usson, Y., Jouk, P.S., Cai, H. Fiber orientation in human fetal heart and ventricular mechanics. 18th World Congress on Medical Physics ad Biomedical Engineering, September 14-19, 1997,Nice, France.

96-1d. Teppaz, P., Herbin, R., **Ohayon, J**. A finite volume method for the simulation of an active fluid-structure interaction in a vascular flow : A 1D model. Euromech 344 : Fluid-Structure Interaction, 11-13 april 1996, Imperial College, London, UK.

95-1d. **Ohayon, J**., Pellissier, S., Roche, M. Contraction of the intestinal tissue. 9th International Congress of Biorheology, july 23-28, 1995, Big Sky, Montana, USA.

92-1d. **Ohayon, J**., Oddou, C., Tedgui, A., Chadwick, R.S. Mechanics of the artery and transmural organization of the arterial wall. 8th Int. Congress of Biorheology 3-8 August, 1992. Yokohama, Japan.

92-2d. Oddou, C., **Ohayon, J**., Pelle, G. Biorheology of the left ventricle and intracardiac hemodynamics. 8th Int. Congress of Biorheology 3-8 August, 1992. Pekin, Chine.

91-1d. Boulos, M., Oddou, C., **Ohayon, J**., Crozatier, B. Numerical model for the left ventricle pump: from the excitation of the fibers to the contraction of the whole heart. 13th IEEE-IMBS; (5):2051-2053, Orlando, Florida, USA, oct 31- nov 3,1991.

90-1d. Chadwick, R.S., Lewkowicz, M., **Ohayon, J**. Nonaxisymmetric effects in ventricular mechanics. 1st World Congress of Biomechanics; (2):60, San Diego, U.S.A., september 1-4, 1990.

89-1d. **Ohayon, J**., Chadwick, R.S. Analysis of biaxial loading of passive myocardial tissue. 7th Int. Congress of Biorheology 18,23 June 1989. Nancy - France. Biorheology 26(3),482, 1989.

88-1d. Chadwick, R.S., **Ohayon, J**. A theory for local myocadial energetics and oxygen demand based on an active rheological law. The Cardiovascular System Society; 89-92, Halifax, Canada, november 7-11, 1988.

86-1d. **Ohayon, J**., Chadwick, R.S. Effects of a radial activation wave in ventricular mechanics. 5th International Conference on Mechanics in Medicine and Biology. Italy, Bologna, July 1-5, 1986.

86-2d. Chadwick, R.S., **Ohayon, J**. A continuum theory for myocardial blood flow. 7th International Conference and Workshop on Cardiovascular System Dynamics. ZUOZ, Switzerland, August 11- 15, 1986.

84-1d. **Ohayon, J**., Rygole, A.L., Pelle, G., Oddou, C. Mechanical model in cardiac mechanics : stresses and pressure distribution inside the left ventricular wall. Workshop on Cardiovascular and Pulmonary Dynamics. Zuoz, Switzerland, August 20-24, 1984.

Congrès Nationaux avec Résumés (n=7)

French National Conferences with Abstracts (n=7)

01-1d. **Ohayon, J**. Rhéologie non-linéaire de la cellule : approche comparative magnétocytométrie / pinces optiques basée sur un modèle aux éléments finis. 19 avril 2001, Institut Albert Bonniot, Grenoble, France.

00-1d. **Ohayon, J**. Biomécanique de la croissance tissulaire modulée par l'organisation cellulaire. École Dynamique et migration cellulaires de l'expérience aux modèles. 10-14 avril 2000, Faculté de médecine de Grenoble, France.

98-1d. **Ohayon, J**., Finet G. Biomécanique de la plaque d'athérosclérose. Congrès des cardiologues Français, Futuroscope, Poitiers, France, 18-19 avril 1998.

93-1d. **Ohayon, J**., Azancot-Benisty A., Chadwick R.S., Ito Y. Interaction ventriculaire : Approche géométrique et biomécanique. Congrès en Echocardiographie et analyse d'images ventriculaires, 25-26 mars 1993, Dijon, France.

85-1d. Brun, P., Vignon, P., Malak, J., Pelle, G., Duburk, F., **Ohayon, J**., Oddou, C. Nouvelles conceptions pour une modélisation du fonctionnement mécanique des fibres myocardiques. Archives des maladies du coeur et des vaisseaux, 78(3):472, 1985.

85-2d. Rygole, A.L., **Ohayon, J**., Pelle, G., Brun, P., Oddou, C. Modèles physiques en vue de l'estimation de paramètres caractéristiques de la performance cardiaque. Archive des maladies du coeur et des vaisseaux, 78 (3):474, 1985.

85-3d. **Ohayon, J**., Rygole, A.L., Pelle, G., Oddou, C., Brun, P. Modélisation de la déformation des vaisseaux coronariens au cours du cycle cardiaque.Archive des maladies du coeur et des vaisseaux, 78 (3):475, 1985.

Brevets (n=4)

Patents (n=4)

2004. Elastography (NIVE): A Non Invasive Vascular Elastography technique based on optical flow (NIVE) (UJF Grenoble / Université de Montréal, n° 2457171. Inventeurs : Maurice R, Cloutier G, **Ohayon J.**, Soulez G.)

2009. Modulographie (iMOD) : Mechanical atherosclerotic plaque characterization using an automatic segmentation procedure based on continuum mechanics (UJF-Grenoble / Université de Lyon, n°08 57929. Inventeurs : **Ohayon J**, Le Floc'h S, Finet G, Tracqui P)

2013. Palpographie (PALPO): Palpation technique for atherosclerotic vulnerable plaque detection: a procedure based on continuum mechanics theory (UJF-Grenoble / Université de Montréal, déposé en 2013. Inventeurs : **Ohayon J**, Deleaval F, Cloutier G)

2013. Inverse Finite Element Code (I-FEM) : A new finite element code for the numerical resolution of inverse problems in elasticity (UJF-Grenoble / Université de Montréal, déposé en 2013. Inventeurs : **Ohayon J**, Bouvier A, Cloutier G)

Publication # 1

Elucidating Atherosclerotic Vulnerable Plaque Rupture by Modeling Cross Substitution of ApoE Mouse and Human Plaque Component Stiffnesses

Ohayon J, Mesnier N, Broisat A, Toczek J, Riou L, Tracqui P

Biomechanics and Modeling in Mechanobiology. 11(6):801-13, **2012**. *(Impact Factor=3.2)*

Abstract: The structure of mouse atherosclerotic lesions may differ from that of humans, and mouse atherosclerotic plaque do not rupture except in some specific locations such as the brachiocephalic artery. Recently, our group was the first to observe that the amplitudes of *in vivo* stresses in ApoE$^{-/-}$ mouse aortic atherosclerotic lesions were much lower and differed from those found in a previous work performed on human lesions. In this previous preliminary work, we hypothesized that the plaque mechanical properties (MP) may in turn be responsible for such species differences. However, the limited number of human samples used in our previous comparative study was relevant but not sufficient to broadly validate such hypothesis. Therefore, in this study, we propose an original finite element strategy that reconstructs the *in vivo* stress/strain (IVS/S) distributions in ApoE$^{-/-}$ artherosclerotic vessel based on cross substitution of ApoE$^{-/-}$ mouse and human plaque components stiffnesses and including residual stress/strain (RS/S). Our results: 1) showed that including RS/S decreases by a factor 2 the amplitude of maximal IVS/S, and more importantly 2) demonstrated that the MP of the ApoE$^{-/-}$ plaque constituents are mainly responsible for the low level - compared to human - of intraplaque stress in ApoE$^{-/-}$ mouse aortic atherosclerotic lesions (8.36 ± 2.63 kPa *versus* 182.25 ± 55.88 kPa for human). Our study highlights that such differences in the distribution and amplitude of vessel wall stress might be one key feature for explaining for the difference in lesion stability between human coronary and mouse aortic lesions.

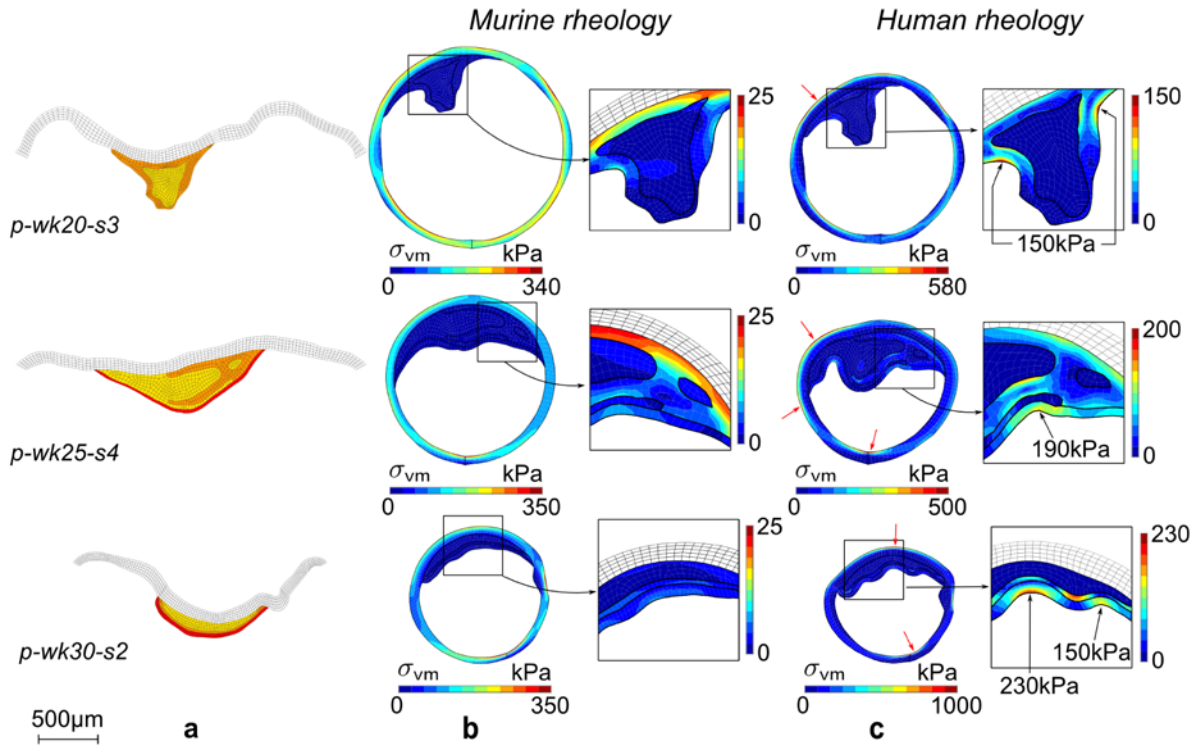

Figure 1: *Influence of the mechanical properties (MP) of the atherosclerotic vessel on the in vivo stress distributions. Finite-Element (FE) simulations were performed for 3 atherosclerotic mouse lesions. Column a: Zero-stress configurations of pathological samples # 3, 4 and 2 for mice of 20, 25 and 30 weeks, respectively (yellow: LiRi regions, orange: HyFb regions, red: CeFb regions, white: arterial wall). Column b) In vivo stress distributions computed by considering the mouse MP. Column c) In vivo stress distributions computed by considering the human MP. A pressure of 14.5 kPa was used for these FE simulations. Red arrows indicate regions with higher stresses.*

Is Arterial Wall-Strain Stiffening and Additional Process Responsible for Atherosclerosis in Coronary Bifurcations? I*n vivo* Study Based on Dynamic CT and MRI

Ohayon J, Gharib AM, Garcia A, Heroux J, Yazdani SK, Malvè M, Tracqui P, Martinez MA, Doblare M, Finet G, Pettigrew RI

American J Physiol Heart Circ Physiol. 301(3):H1097-106, **2011.** *(Impact Factor: 3.7)*

Abstract: Coronary bifurcations represent specific regions of the arterial tree that are susceptible to atherosclerotic lesions. While the effects of vessel compliance, curvature, pulsatile blood flow and cardiac motion on coronary endothelial shear stress have been widely explored, the effects of myocardial contraction on arterial wall stress/strain (WS/S) and vessel stiffness distributions remain unclear. Local increase of vessel stiffness resulting from wall-strain stiffening phenomenon – a local process due to the nonlinear mechanical properties of the arterial wall – may be critical in the development of atherosclerotic lesions. Therefore, the aim of this study was to quantify WS/S and stiffness in the coronary bifurcations and to investigate correlations with plaque sites. Anatomic coronary geometry and cardiac motion were generated based on both computer tomography and magnetic resonance imaging examinations of eight patients with minimal coronary disease. Computational structural analyses using finite element method were subsequently performed and spatial luminal arterial wall stretch ($LW_{stretch}$) and stiffness (LW_{stiff}) distributions in the left main coronary bifurcations were calculated. Our results show that all plaque sites were concomitantly subject to high $LW_{Stretch}$ and high LW_{Stiff}, with mean amplitudes $34.7 \pm 1.6\%$ and 442.4 ± 113.0 kPa, respectively. The mean LW_{Stiff} amplitude was found slightly greater at the plaque sites on the left main coronary (mean value, 482.2 ± 88.1 kPa) as compared to those computed on the left anterior descending and left circumflex coronaries (416.3 ± 61.5 kPa and 428.7 ± 181.8 kPa, respectively). These finding suggests that local wall stiffness plays a role in the initiation of atherosclerotic lesions.

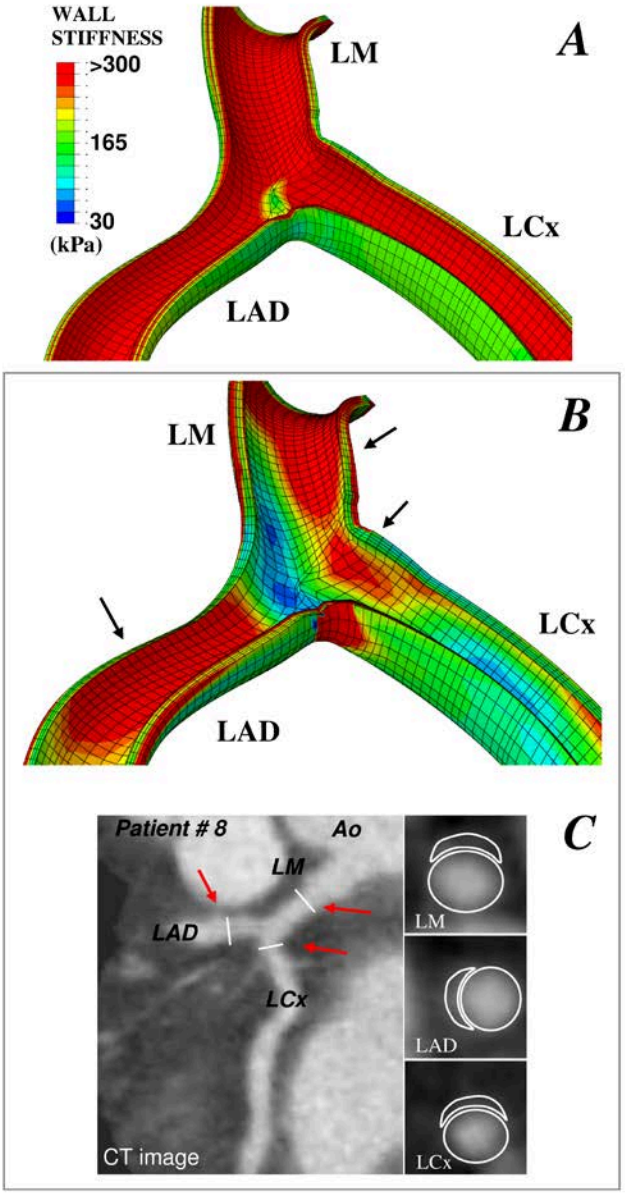

Figure 2: *Influence of cardiac contraction on the spatial distribution of the arterial wall stiffness (unit: kPa). Results show spatial wall stiffness distribution when neglecting (A) and considering (B) heart motion. All these computations were performed on patient # 8. C) CT views highlighting lesion sites and showing the cross-section for plaques located in LM, LAD and LCx branches. Arrows indicate lesion sites.*

On the Potential of a New IVUS Elasticity Modulus Imaging Approach for Detecting Vulnerable Atherosclerotic Coronary Plaques: In Vitro Vessel Phantom Study

Le Floc'h S, Cloutier G, Finet G, Tracqui P, Pettigrew RI, Ohayon J

Physics in Medicine & Biology, 55:5701-5721, **2010**. (Impact factor: 3.2)
(International Patent on " Image processing for evaluating the risk of atheroma plaque rupture")

Abstract: Peak cap stress amplitude is recognized as a good indicator of vulnerable plaque (VP) rupture. However, such stress evaluation strongly relies on a precise, but still lacking, knowledge of the mechanical properties exhibited by the plaque components. As a first response to this limitation, our group recently developed an original theoretical approach, called iMOD, which reconstructs elasticity maps (or modulograms) of atheroma plaques from the estimation of strain fields. In the present *in vitro* experimental study, conducted on PVA-C arterial phantoms, we investigate the benefit of coupling the iMOD procedure with the acquisition of intravascular ultrasound (IVUS) measurements for detection of VP. Our results show that the combined iMOD-IVUS strategy : 1) successfully detected and quantified soft inclusion contours with high positive predictive values and sensitivities of 89.7 ± 3.9% and 81.5 ± 8.8 %, respectively, 2) estimated reasonably cap thicknesses larger than ~300 µm, but underestimated thinner caps 3) quantified satisfactorily Young's modulus of hard medium (mean value of 109.7 ± 23.7 kPa instead of 145.4 ± 31.8 kPa), but overestimated the stiffness of soft inclusions (mean Young`s moduli of 31.4 ± 9.7 kPa instead of 17.6 ± 3.4 kPa). All together, these results demonstrate a promising benefit of the new iMOD-IVUS clinical imaging method for *in vivo* VP detection.

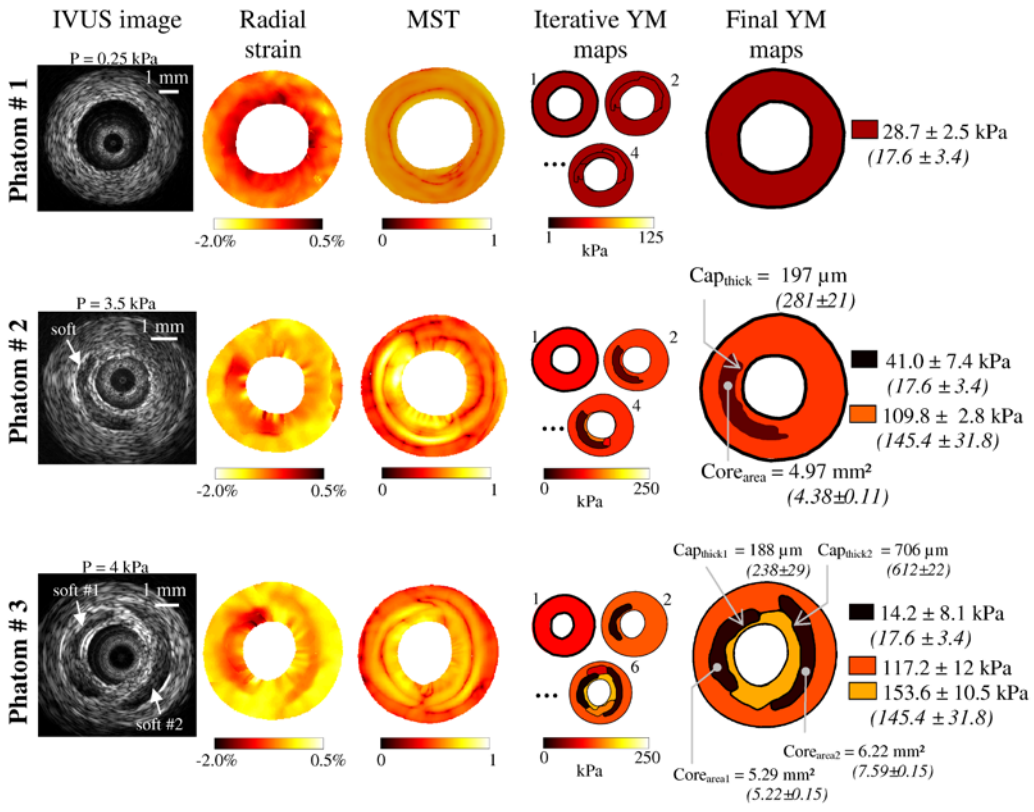

Figure 3: *Performance of our method to detect soft inclusions using experimental IVUS images acquired on the three PVA-C phantoms. Column 1: IVUS images. Column 2: Estimated radial strain fields obtained by using the Lagrangian Speckle Model Estimator (LSME). Column 3: Spatial pseudo-gradient elasticity field resulting from the modified Sumi's transform (MST) procedure. Column 4: Evolution of the Young's modulus (YM) map obtained during the iterative process combining the dynamic Watershed segmentation and optimization procedures. Column 5: Simplified final Young's modulus maps and resulting estimations of cap-thicknesses (Cap_{thick}) and necrotic core areas ($Core_{area}$). In parenthesizes are given the real histomorphometric measurements and Young's moduli values measured by atomic force microscopy (AFM) in our laboratory.*

Necrotic Core Thickness and Positive Arterial Remodeling Index: Emergent Biomechanical Factors for Evaluating the Risk of Plaque Rupture

Ohayon J, Finet G, Gharib AM, Herzka DA, Tracqui P, Heroux J, Rioufol G, Kotys MS, Elagha A, Pettigrew RI

American J Physiol Heart Circ Physiol., 295(2):H717-27, **2008**. *(Impact Factor=3.7)*

Abstract : Fibrous cap thickness (Cap_{thick}) is often considered as diagnostic of the degree of plaque instability. Necrotic core area ($Core_{area}$) and the arterial remodeling index ($Remodi_{ndex}$), on the other hand, are difficult to use as clinical morphological indices: literature data show a wide dispersion of Core-area thresholds above which plaque becomes unstable. Although histopathology shows a strong correlation between $Core_{area}$ and $Remod_{index}$, it remains unclear how these interact and affect peak cap stress (Cap_{stress}) - a known predictor of rupture. The aim of this study was to investigate the change in plaque vulnerability as a function of necrotic core size and plaque morphology. Cap_{stress} value was calculated on 5,500 idealized atherosclerotic vessel models, which had the original feature of mimicking the positive arterial remodeling process described by Glagov. Twenty four non-ruptured plaques acquired by IVUS on patients were used to test the performance of the associated idealized morphological models. Taking advantage of the extensive simulations, we investigated the effects of anatomical plaque features on Cap_{stress}. It was found that: (i) at the early stages of positive remodeling, lesions were more prone to rupture, which could explain the progression and growth of clinically silent plaques; and (ii) in addition to cap thickness, necrotic core thickness - rather than area - was critical in determining plaque stability. This study demonstrates that plaque instability is to be viewed not as a consequence of fibrous cap thickness alone, but rather as a combination of cap thickness, necrotic core thickness and the arterial remodeling index.

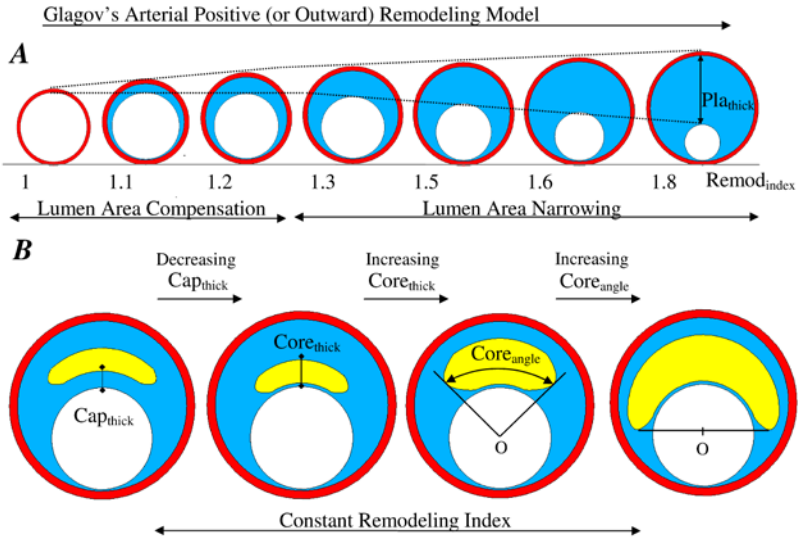

Figure 4A: *Atherosclerotic vessel-growth model used in the computational simulations - A) Schematic description of the positive coronary remodeling described by Glagov et al. and included in our model. Pla_{thick}: plaque thickness; $Remod_{index}$: arterial remodeling index. B) For a given remodeling index, the main parameters describing plaque morphology – i.e., cap thickness (Cap_{thick}), necrotic core thickness ($Core_{thick}$) and necrotic core arc angle ($Core_{angle}$) – were varied. A total of 5,500 distinct plaque geometries were considered. Red: arterial wall; blue: fibrosis; yellow: necrotic core.*

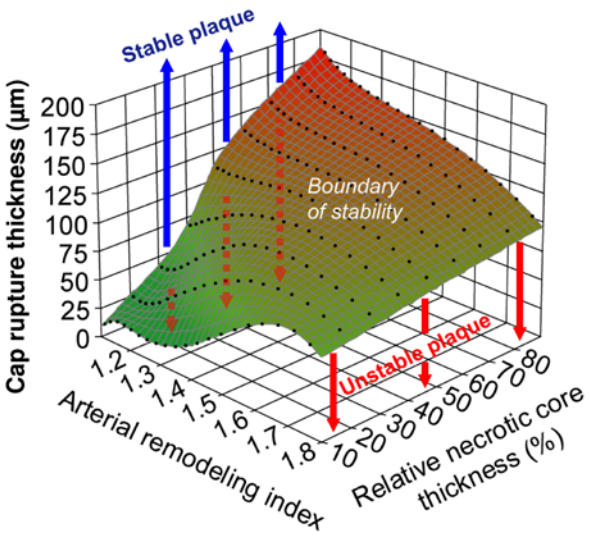

Figure 4B*: Three-dimensional plot highlighting the influences of remodeling index and relative necrotic core thickness on critical cap thickness. The critical cap thickness is defined as the value at which cap stress reaches the critical or rupture point tensile stress. This result shows that there is no single such threshold, which rather depends strongly on remodeling index and relative necrotic core thickness.*

Influence of Residual Stress/Strain on the Biomechanical Stability of Vulnerable Coronary Plaques: Potential Impact for Evaluating the Risk of Plaque Rupture

Ohayon J, Dubreuil O, Tracqui P, Le Floc'h S, Rioufol G, Chalabreysse L, Thivolet F, Pettigrew RI, Finet G

American J Physiol Heart Circ Physiol., 293(3):H1987-96, **2007**. *(Impact Factor=3.7)*

Abstract: In a vulnerable plaque (VP), rupture often occurs at a site of high stress within the cap. It is also known that vessels do not become free of stress when all external loads are removed. Previous studies have shown that such residual stress/strain (RS/S) tends to make the stress distribution more uniform throughout the media of a normal artery. However, the influence of RS/S on the wall stress distribution in pathological coronaries remains unclear. The aim of this study was to investigate the effects of RS/S on the biomechanical stability of VPs. RS/S patterns were studied ex vivo in six human vulnerable coronary plaque samples. Since the existence of RS/S can only be assessed by releasing it, the opening angle technique was the experimental approach used to study the geometrical opening configurations of the diseased arteries, producing an arterial wall in a near-zero stress state. Reciprocally, these opening geometries were used in finite element simulations to reconstruct the RS/S distributions in closed arteries. It was found that the RS/S: i) is not negligible, ii) dramatically affects the physiological peak stress amplitude in the thin fibrous cap, iii) spotlights some new high stress areas, and iv) could be a landmark of the lipid core's developmental process within a VP. This study demonstrates that plaque rupture is not to be viewed as a consequence of intravascular pressure alone, but rather of a subtle combination of external loading and intraplaque RS/S.

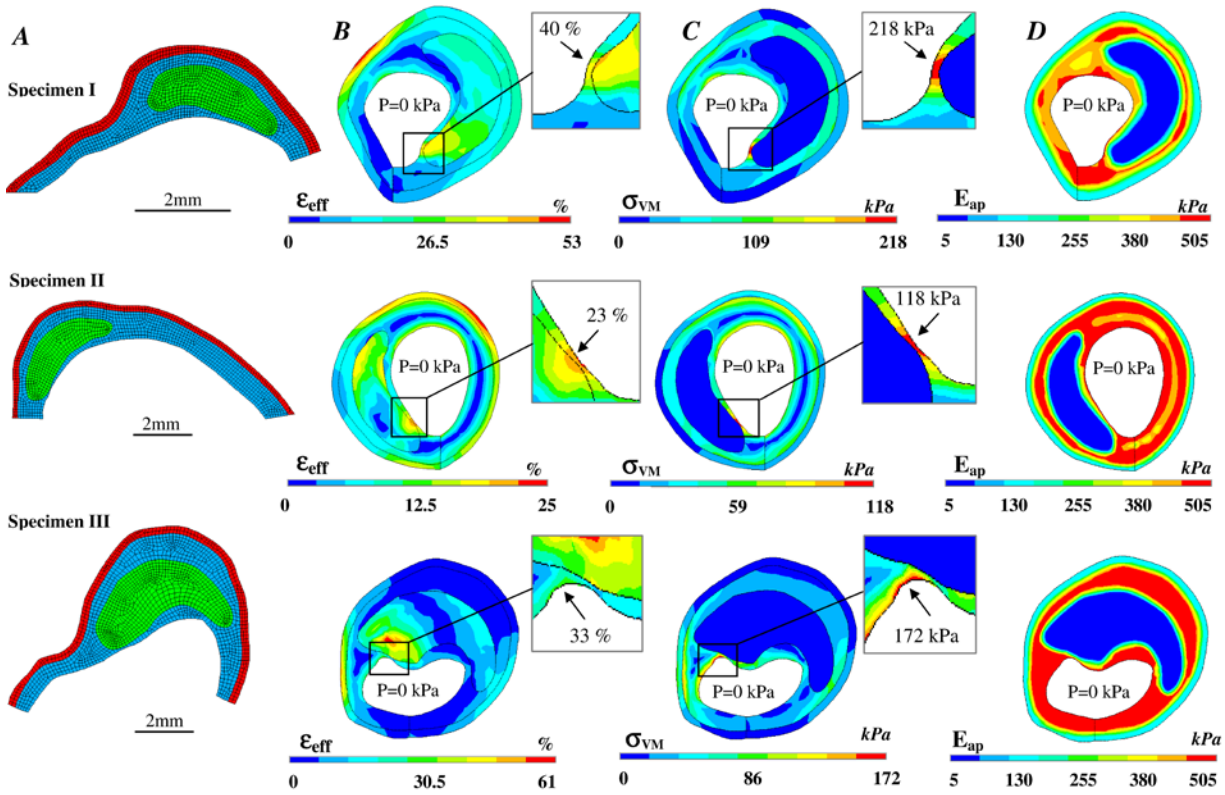

Figure 5*: Color maps of finite element results highlighting, for specimens I, II and III, the residual strain and stress distributions in the vulnerable coronary plaque.* ***A)*** *geometries, meshes and plaque constituents of the zero-stress configurations used to initiate the numerical computations for the three first specimens. Green: lipid core; blue: cellular fibrosis; red: arterial wall.* ***B)*** *spatial distribution of effective mean residual strain* ε_{eff}. ***C)*** *spatial distribution of von-Mises residual stress* σ_{VM} *(unit: kPa; 1kPa= 0.1333 mmHg).* ***D)*** *color maps giving spatial distribution of the* $E_{ap}= \sigma_{VM}/\varepsilon_{eff}$ *ratio (unit: kPa), which reflects the apparent stiffness of the tissue. Vulnerable thin fibrous cap sites of interest are zoomed for clarity.*

In Vivo Prediction of Coronary and Carotid Atherosclerotic Plaque Mechanical Rupture: Progress, Challenges, and New Directions

Jacques Ohayon, Professor of Mechanics
University of Savoie, Polytech Annecy-Chambéry, France
Laboratory TIMC/DyCTiM - IMAG, UJF, CNRS UMR 5525, Grenoble, France

Contents

1. Societal Issues and Relevance of my Interdisciplinary Research
2. My Expertise and Leadership in Biomechanics of Plaque Rupture
2.1 Mechanical factors responsible for atherosclerotic plaque initiation
2.2 Mechanical factors responsible for atherosclerotic plaque rupture
3. New *in Vivo* Technique for Mechanical Characterization of Vulnerable Atherosclerotic Plaques
4. Bibliography

1. SOCIETAL ISSUES AND RELEVANCE OF THIS INTERDISCIPLINARY RESEARCH

Cardiovascular disease remains the number one killer in developed countries. Recent estimations performed on the American population indicate that approximately 82 600 000 patients suffer of one or several types of cardiovascular pathologies (*Roger 2012*), coronary heart disease and stroke being the primary ones. Acute coronary syndromes and/or sudden cardiac death, both caused by the rupture of a vulnerable coronary plaque, are responsible for more than 1 million cardiac events every year in the United States and 19 millions worldwide (*Naghavi 2003, Roger 2012*). In addition, stroke is the third cause of death (134,000 each year in the USA) and the leading cause of morbidity (*Roger 2012*). More than 60% of all cerebral infarctions are caused by the rupture of a vulnerable plaque (VP)[1] (*Loyd-Jones 2009*). Among individuals with coronary or carotid artery disease, only a minority experience warning symptoms, the majority having their event from previously asymptomatic lesions (*Nicolaides 2003*). Moreover, the occurrence of cardiovascular diseases is much higher for diabetic individuals and the size of this population of patients is expected to increase exponentially over the course of the next decade (*Eckel 2005*).

The imbalance of stabilizing and destabilizing forces within the lesion play a role in the mechanisms of plaque rupture, plaque erosion and intra-plaque hemorrhage (*Ohayon 2001*, *Finet 2004*)[2]. Thus, studies focusing on the biological mechanisms leading to plaque vulnerability and rupture represent a field of research with intense on-going activity. However, considering both the well-recognized influence of mechanical factors on fundamental cellular processes (*Lehoux 2006*) and the fact that plaque rupture is by essence due to mechanical instability, **the analysis of the spatiotemporal evolution of mechanical stresses during atherogenesis appears crucial as well for understanding why and how development and rupture of a VP occurs.**

Understanding the evolution of atherosclerotic plaque vulnerability and increasing knowledge of the plaque growth process through the combined use of mechanical modeling based on the nonlinear continuum mechanics theory, finite element method, together with clinical and biological investigations, were my main fields of interest and investigation during this last 10 years. Since 2001, I published in international journals 55 biomechanical studies on the atherosclerotic VP rupture and on the mechanical characterization of biological tissues. My contribution is today well recognized by my interdisciplinary scientific international community. **The success of my research performed on "Biomechanics of Plaque Rupture" was also due to my abilities to dialogue, motivate and regroup scientists from different fields (Mechanics, Mathematics, Cardiology, Biology, Pathology and Image analysis) to work together.** Some of my remarkable findings, contributions and important events are briefly mentioned below.

[1] Nomenclature: VP: Vulnerable plaque - IVUS: Intravascular ultrasound - OCT: Optical coherence tomography
[2] In this proposal, articles from my group are *underlined*.

In 2001, we were the first group in the world demonstrating that it was possible to predict *in vivo* the human coronary plaque rupture location using intravascular ultrasound (IVUS) and structural mechanical analysis (*Ohayon 2001*).

In 2006, I was personally invited by the Director of the National Institute of Biomedical Imaging and Bioengineering (NIBIB) at the National Institutes of Health (NIH) - Bethesda MD - USA, Dr Roderic I. Pettigrew (*http://www.nibib.nih.gov/About/Directories/Pettigrew*), to spend one year (as a senior visiting scientist) **in his laboratory in order to create and coordinate an interdisciplinary international consortium on Biomechanics of Atherosclerosis[3] regrouping experts in Radiology, Cardiology, Biology, Mechanics, Mathematics, Pathology and Image analysis**.

In 2006 and 2008, I was invited by the Spanish Ministry of Science and Innovation to perform a series of 18 post-doctoral lectures, for scientists from Madrid, Valence, Barcelona and Zaragoza universities, on "*Biomechanics of Atherosclerosis and Mechanical Characterization of Biological Tissues* ".

In 2010, we were the first group in the world reconstructing fully automatically and *in vitro* - i.e. without any manual segmentations - the Young's modulus map from real IVUS sequences (acquired with a Galaxy II IVUS system of Boston Scientific Inc., USA) by using vascular polyvinyl alcohol cryogel arterial phantoms (*Le Floc'h 2009, 2010 and Patent iMOD 2009*).

In 2011, I was invited with my collaborator Dr G. Finet (from the Cardiologic Hospital of Lyon - France) by the President of the International Biotechnology Company Boston Scientific Inc. (Minneapolis-USA) to visit their coating stent factory and to present our biomechanical studies in progress on plaque rupture, hemodynamic perturbation due to stent apposition, and plaque elasticity reconstruction.

In 2012, we were the first group in the world reconstructing fully automatically and from *in vivo* IVUS sequences acquired on 12 patients in Japan by Dr Y. Saijo (Tohoku University, Sendai, Japan) the Young's modulus map of VPs scanned by IVUS (see Fig. 4 section 3.1) (*Le Floc'h 2012*).

In 2012 also, the American College of Cardiology Foundation published - in their famous ***JACC-Cardiovascular Imaging*** **journal** - the international report of the National Heart, Lung, and Blood Institute (NHLBI) working group (in which I was a member) on detection of high-risk atherosclerotic plaque (*Fleg 2012*). Indeed, in June 9th 2009, I was invited with 13 international scientists and clinical experts, to take part in a NHLBI Working Group (NIH, Bethesda, MD, USA), to examine the current state of the art in the identification of high-risk atherosclerotic plaque and provide recommendation for future research. We first discussed the PROSPECT (Providing Regional Observation to Study Predictor of Events in the Coronary Tree) study (*Stone 2011*) and related natural history studies, we then reviewed the pathological basis for high-risk-plaques, invasive and noninvasive imaging modalities, biomarkers that may help to identify high-risk patients, animal models of coronary atherosclerosis, biomechanical factors for evaluating the risk of plaque rupture, and finally concluded with the following identification of future research priorities and recommendations (*Fleg 2012*): (1) Improve understanding of the plaque microenvironment in the pathogenesis of plaque instability; (2) Develop and validate molecular and genetic markers of VP; and (**3) Develop and validate noninvasive and invasive imaging technique to identify, monitor and treat VPs.**

In 2013, I developed, in collaboration with scientists of my international consortium[3], 2 patents to characterize the compliance of a VP by using a IVUS-palpography approach (patent named PALPO) (*Deleaval 2013*), and to solve an inverse problem in elasticity by using a direct approach based on a new Inverse Finite Element Method (patent named I-FEM) (*Bouvier 2013*).

In 2013 also, the consortium that I coordinate was invited by the editors in Chief of 3 international Journals (namely: "***Journal of Biomechanics***", "***Annals of Biomedical Engineering***" and "***Computerized Medical Imaging and Graphics*** ") to submit 3 invited papers in their Special Issues on "Atherosclerotic Plaque Rupture" (*Ohayon 2013, Riou 2013, Mercure 2013*).

---

[3] The active international consortium that I created and coordinate since 2007 is composed of: National Institutes of Health (NIH), MD, USA (Drs R.I. Pettigrew, MD, PhD and A.M. Gharib, MD, **CT and MRI Imaging experts**) - University of Montréal, Canada (Drs G. Cloutier, PhD and G. Soulez, MD, PhD, **MRI imaging and Ultrasound experts**, respectively) - University of Tohoku, Japan (Dr Y. Saijo, MD, PhD, **Acoustic Microscopy expert**) - University of Zaragoza, Spain (Drs M. Malvé, PhD, M.A. Martinez, PhD and E. Pena, PhD, **Applied Fluid and Solid Mechanics experts**) - EPFL University of Lausanne, Switzerland (Dr. M. Stuber, PhD, **MRI expert**)- University of South Alabama, USA (Dr. S.K. Yazdani, PhD, **Tissue Engineering expert**) - University of Lyon, France (Drs. G. Rioufol, MD, PhD and G. Finet, MD, PhD, **IVUS and OCT Imaging experts**) - University of Grenoble, France (Dr. L. Riou, PhD, **Biology expert**) - University of Rochester, NY, USA (Dr. M.M. Doyley, PhD, **Applied Physics and Mathematics expert**).

2. MY EXPERTISE AND LEADERSHIP IN BIOMECHANICS OF PLAQUE RUPTURE

Atherogenesis, i.e. the initiation and growth of atherosclerotic plaques, is determined by biological processes consisting mainly of (Fig. 1A) (1) the infiltration and accumulation of low-density lipoproteins **(**LDL) in the subendothelial space, (2) the recruitment of circulating inflammatory cells such as monocytes and lymphocytes at the site of plaque development, and (3) the migration and proliferation of smooth muscle cells from the media into the intima. The inflammatory reaction is responsible for the formation of a lipidic and necrotic core surrounded by a fibrous cap. When a VP undergoes rupture (i.e., when fibrous cap ruptures), luminal thrombus formation is prompted by the interaction between intraplaque thrombogenic components and the blood. Thrombus formation is responsible for the clinical symptoms of a coronary event.

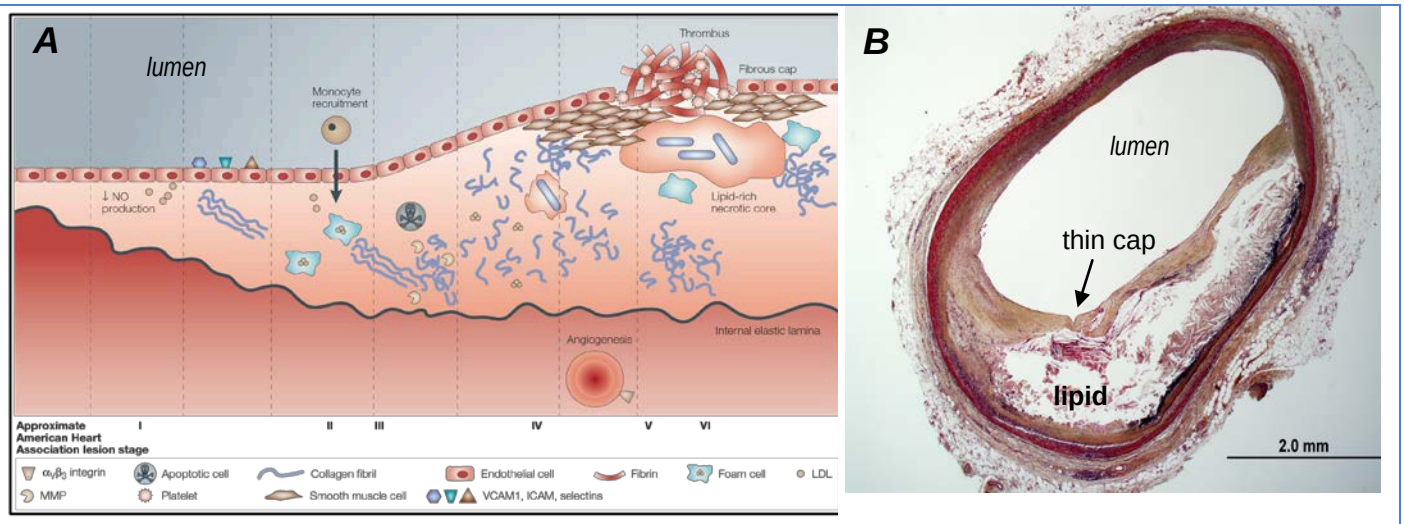

FIGURE 1. A) Illustrative sequence of processes involved in atherogenesis, starting with pre-lesional endothelial dysfunction (left) through monocyte recruitment to the development of advanced plaque complicated by thrombosis (right). The mechanisms are grossly simplified but focus on components (for example, cell adhesion molecules, macrophages, connective tissue elements, lipid core and fibrin) and processes (for example, apoptosis, proteolysis, angiogenesis and thrombosis) in plaques that have been imaged or that present useful potential imaging targets. ICAM, intercellular cell adhesion molecule; LDL, low-density lipoprotein; MMP, matrix metalloproteinase; NO, nitric oxide; VCAM, vascular cell adhesion molecule (from *Choudhury 2004*). B) Histological view of a human vulnerable coronary plaque cross-section with a large extracellular lipid core (lipid) and a thin fibrous cap (*Courtesy of Dr R. Virmani from the CvPath, Gaithersburg, MD, USA*).

2.1. MECHANICAL FACTORS RESPONSIBLE FOR ATHEROSCLEROTIC PLAQUE INITIATION

Although the coronary and peripheral systems are in their entirety exposed to the same atherogenic cells and molecules in the plasma, atherosclerotic lesions form at specific regions of the arterial tree. The coronary wall is constantly subjected to both shear stress due to blood flow and wall strain/stress induced by pulsatile blood pressure and heart motion. Like most biological materials, vascular wall stiffens as it is stretched. I underlined, for the first time, the importance of local arterial wall stiffness in the development of atherosclerosis and showed that luminal wall stiffness might, in addition to low endothelial shear stress (*Chatzizisis 2007, Malvè 2011*) and cyclic wall stretch (*Lehoux 1998*), be a precondition for the development of atherosclerosis (*Ohayon 2011*). Patients with minimal coronary disease, having undergone both computer tomography (Fig. 2A) and magnetic resonance imaging examinations, were enrolled for this study during my sabbatical in 2007 at the National Institutes of Health (NIH, Bethesda, MD, USA). Nonlinear structural analysis was performed by using the Holzapfel's anisotropic hyperelastic constitutive law (*Holzapfel 2005*) to investigate the effects of cardiac motion and blood pressure on spatial luminal arterial wall stretch and stiffness (LW_{stiff}) distributions in the left main coronary bifurcations. In addition, a computational fluid dynamic analysis was performed to quantify endothelial shear stress (ESS) (Fig. 2B). Our results indicated that 89% of lesions were located in specific regions of high luminal wall stiffness (300 kPa < LW_{Stiff} < 800 kPa) (Fig. 2C) and low ESS (< 1Pa). Although further studies are needed to extend the present work, our results suggest that atherosclerosis is to be viewed not as a consequence of ESS alone, but rather as a combination of low ESS, cyclic wall stretch and high arterial wall stiffness.

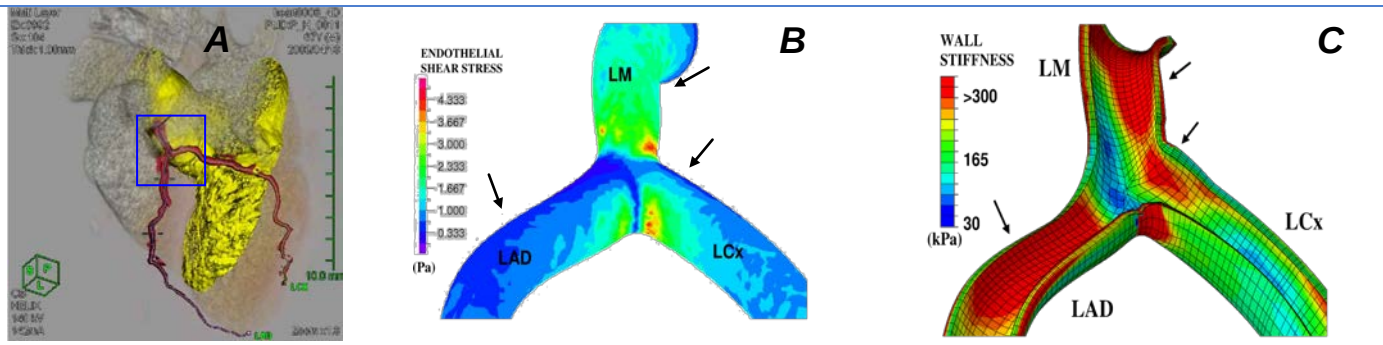

FIGURE 2. A) Computer tomography view of the left main coronary bifurcation from which the 3D reconstruction of the coronary bifurcation was extracted. The square indicates the studied region (from *Ohayon 2011*). B) Computational fluid dynamics results highlighting the spatial distributions of endothelial shear stress (from *Malvè 2011*). C) Results showing the spatial wall stiffness distribution. Arrows indicate plaque sites located in LM, LAD and LCx branches (from *Ohayon 2011*). LM: Left main artery; LAD: Left anterior descending artery; LCx: Left circumflex artery. All these computations were performed on the same coronary bifurcation.

2.2. MECHANICAL FACTORS RESPONSIBLE FOR ATHEROSCLEROTIC PLAQUE RUPTURE

Scientists from 46 institutions around the world joined their expertise to better understand which VP at risk of thrombotic complications would cause fatal events (*Naghavi 2003*). A VP at risk of rupture was defined, by this group of expert scientists, as a lipidic (or necrotic) core accounting for >40% of the plaque's total volume that is covered by a thin-cap fibroatheroma <100 µm (Fig. 1B). Due to inflammation and the repetitive cycling movement of the artery, the fissure of the fibrous cap adjacent to the vessel lumen would promote the cascade of coagulation and the formation of a blood clot occluding the flow of blood. Plaque rupture (i.e., dissection, fissuring or ulceration) is the most common type of complication, accounting for close to 70% of all serious episodes. Nonruptured plaques account for ≈ 30% of all fatal outcomes (*Naghavi 2003*). Plaque erosion (i.e., a lesion with no evidence of dissection or cleft), intra-plaque hemorrhage and others circumstances such as hypercoagulable "vulnerable blood" would explain sudden thrombotic occlusions in these nonruptured plaques (*Naghavi 2003*). A heavily calcified plaque is significantly less likely to be vulnerable and symptomatic than a non-calcified plaque (*Nandalur 2005*) but specific locations of calcified nodules could predict vulnerability (e.g., calcium nodules close to the vessel lumen) (*Vengrenyuk 2006, Maldonado 2012*). Fragile vasa-vasorum neovascularisation is also seen as a vulnerable condition (*Granada 2008*). Note that the above mentioned working group (*Naghavi 2003*) recognized also the importance of studying the mechanical stability of the plaque.

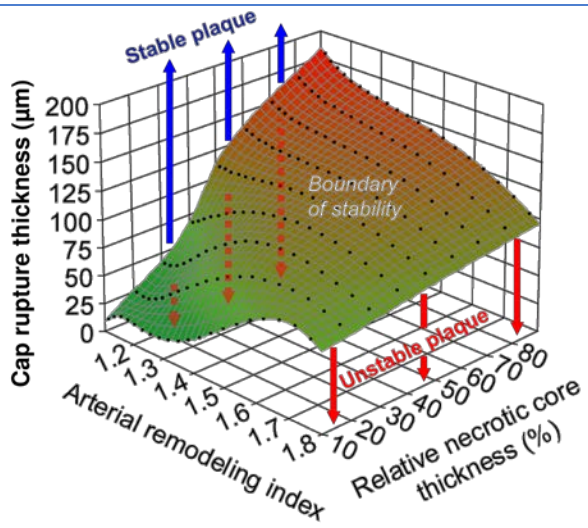

FIGURE 3. Three-dimensional plot illustrating the relationship between remodeling index RI (young plaques have a RI close to 1 while mature ones have a RI close to 1.8), relative necrotic core thickness and cap rupture thickness (or critical cap thickness). The critical cap thickness is defined as the value at which cap stress reaches the critical or rupture point tensile stress of 300 kPa. Interestingly, plaques with low remodeling index and a large relative necrotic core thickness can be seen to be more prone to rupture, with a high critical cap thickness. The domains below (red arrows) and above (blue arrows) the boundary of stability highlight the features of unstable and stable vulnerable plaques, respectively (*Ohayon 2008, Fleg 2012, Ohayon 2013*).

Intravascular ultrasound (IVUS) (*Rioufol 2002*), optical coherence tomography (OCT) (*Kubo 2007*), computed tomography (CT) (*Fayad 2002*), and magnetic resonance imaging (MRI) (*Kotys 2009*) look promising because of the ability of these methods to image the coronary and carotid walls. These imaging techniques are used to detect VPs but they did not succeed so far to prospectively predict plaque rupture. Thus, the determination of morphological clinical criteria based on imaging of the lesion still provides rather imprecise and insufficient predictors of risk. Additional mechanical factors must be taken into consideration to extend our knowledge of the VP rupture process (*Virmani 2000*).

In such a context, I found that (Fig. 3): (1) at the early stages of positive remodeling (i.e., for young plaques), lesions were more prone to rupture, which could explain the progression and growth of clinically silent plaques; and (2) in addition to cap thickness, necrotic core thickness - rather than area - was critical in determining plaque stability. Thus plaque instability is to be viewed not as a consequence of fibrous cap thickness alone, but rather as a combination of cap thickness, necrotic core thickness and the arterial remodeling index.

3. NEW *IN VIVO* TECHNIQUES FOR MECHANICAL CHARACTERIZATION OF VULNERABLE ATHEROSCLEROTIC PLAQUES

The challenge for the new generation of *in vivo* clinical imaging methods is that prediction of the vulnerable atheroma plaque rupture requires not only an accurate description of plaque morphology (*Farb 1996, Ohayon 2008*), but also a precise knowledge of mechanical properties of plaque constituents (*Ohayon 2012*). Indeed, such knowledge will likely allow a precise evaluation of the thin-cap fibro-atheroma peak stress amplitude, which is a reliable predictor of plaque rupture (*Ohayon 2001 , Finet 2004, Ohayon 2007*). The clinical success of a surgical intervention depends on knowledge of whether a carotid or coronary lesion is at risk for rupture and can be responsible for the development of neurological or cardiovascular events, respectively. The medical history and paraclinical tests are sometimes insufficient to resolve this uncertainty. **Hence, it is essential to develop, test and validate novel invasive and noninvasive clinical diagnostic tools based on continuum mechanics combining strain-elastography (i.e. strain map) and modulography (i.e. elasticity map) techniques for a better *in vivo* evaluation of the risk of vulnerable carotid and coronary plaque ruptures.**

The following proposal focuses mainly on the development of new generation of clinical tools based on continuum mechanics theory and mathematical resolution of inverse problems in elasticity for the prediction of the vulnerable plaque rupture. This proposal falls within the scope of one of the three major future research recommendations proposed by the international board of the NHLBI working group (*Fleg 2012*), which is to develop and validate novel mechanical techniques based on clinical image sequences to detect, identify and diagnose atherosclerotic lesions vulnerable to rupture.

In such spirits of designing new tools and solving inverse problems in elasticity for *ex vivo* and *in vivo* mechanical characterization and detection of atherosclerotic plaques, and for a better diagnosis of cardiovascular and stroke events, several approaches were proposed (*Doyley 2012*).

The virtual histology technique, based on the parametric spectral analysis of the radio-frequency ultrasound backscattered echoes, was developed by Volcano Therapeutics Inc. and by Boston Scientific Inc. However, such technique does not allow any accurate quantification of the mechanical properties of the plaque constituents which are essential for the computation of intraplaque stresses. Moreover, *Thim et al.* (2010), in their recent study performed on adult atherosclerosis-prone minipigs, found no correlation between necrotic core size determined by virtual and real histology, questioning the ability of virtual histology to detect rupture-prone plaques.

In 2004, I developed and **patented**, in collaboration with Canadian scientists (Drs G. Cloutier and G. Soulez, University of Montreal), robust strain-elastography approaches based on optical flow method to estimate, with ultrasound, the radial strain within the vascular wall induced by the natural cardiac pulsation (*Maurice 2004a*). However, these methods did not overcome a main limitation related to the complex geometries of atherosclerotic plaques, which alter the intraplaque strain fields and inhibit direct translation into plaque mechanical properties.

Computation of such modulograms (i.e., elasticity maps) is a challenge that has been tackled by a rather large diversity of approaches. Based on the estimation of the strain field inside the atheroma plaque obtained with various ultrasound-based techniques (*de Korte 2002, Maurice 2004b*), studies have been performed to estimate vascular elasticity maps. Either direct approaches (*Kim 2004, Kanai 2003*) or iterative procedures (*Baldewsing 2007, Luo 2006*) were proposed to solve such inverse problem. The iterative approaches used a central core optimization algorithm to minimize the error between computed and measured strains or displacement fields. For such approaches, improvement of plaque elasticity reconstruction depends on the performance of the optimization procedure and the accuracy of the given contours of all plaque constituents. Thus, several groups (*Soualmi 1997, Khalil 2006*) developed robust optimization algorithms for extracting elastic moduli of coronary and carotid plaque components, assuming a known plaque morphology. Originally, Baldewsing *et al.* (*2006*) developed a parametric finite element model (PFEM) to assess the plaque morphology. Interestingly, this approach has been extended by the same group to the case of multiple necrotic cores: each core was considered separately and the mechanical solution was obtained by considering the superposition of non correlated inverse problems (*Baldewsing 2007*). Despite its robustness, this PFEM has some limitations. Indeed, this method neglects the mechanical interaction between

inclusions. Therefore, such PFEM would not be efficient enough to extract the real plaque morphology exhibiting several neighboring necrotic cores and heterogeneous structures including smooth muscle cells, collagen-rich fibrotic tissues and/or calcium inclusions, thus preventing a good diagnosis of plaque vulnerability.

In 2009, in collaboration with Dr. G. Finet (Cardiologic Hospital of Lyon, France), and with my post-doc (Simon Le Floc'h) we developed and **patented** a novel PFEM (named iMOD for imaging modulography) based on an original pre-conditioning step for the optimization process, and a new approach combining a dynamic watershed segmentation method with a mathematical optimization procedure to extract the morphology and Young's modulus of each plaque component (*Le Floc'h 2009*).This combined approach, based on the continuum mechanics theory, was applied to simulated images of VPs.

In 2010, my group conducted *in vitro* polyvinyl alcohol cryogel (PVA-C) vascular phantom experiments with IVUS acquisitions (Galaxy II system with Atlantis SR Pro 3.6F at 40Mhz; Boston Scientific, USA) to investigate on the potential of our new IVUS elasticity modulus imaging approach (*Le Floc'h 2010*).

In 2012, *in vivo* modulography of human coronaries partially corroborated by histology (atherectomy) was presented for the first time in the world (Fig. 4) (*Le Floc'h 2012*).

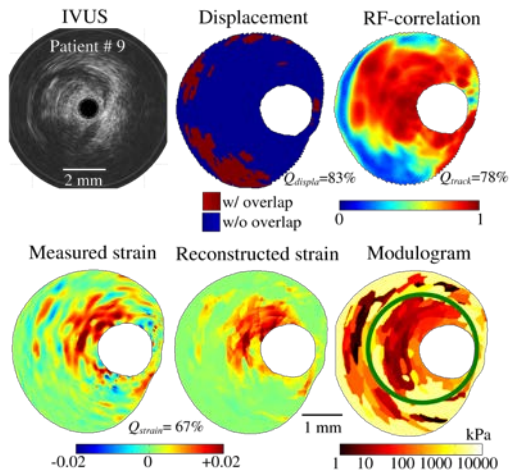

FIGURE 4. Promising preliminary *in vivo* results showing the performance of our plaque elasticity reconstruction model iMOD to extract morphology and elasticity map from the IVUS sequence of a patient. Notice that regions with tissue overlap, observed in the displacement map, correlate well with low radio frequency RF-correlation coefficient sites. The high value of the strain quality index found (Q_{strain}=67%) indicates that the method reproduced accurately (in 67% of the total plaque area) the measured radial strain field. The green contour in the modulogram corresponds to the boundary of the lesion that was excised during the directional coronary atherectomy procedure (from *Le Floc'h 2012* and *Patent iMOD 2009*).

In 2013, we revisited the elasticity-palpography technique (E-PT) proposed initially by Céspedes *et al.* (2000) and **patented** the corrected approach (named PALPO) (*Deleaval 2013*). From the IVUS strain images, Céspedes *et al.* (2000) proposed an E-PT to estimate the apparent stress-strain modulus (S-SM) palpogram of the thick endoluminal layer of the arterial wall. However, this approach suffers of two major limitations: **(i)** it was developed for non realistic homogeneous, circular and concentric VPs, and **(ii)** it is difficult, with such a simplified model, to correlate the resulting S-SM to the real Young's modulus distribution in the palpography domain. The present study was therefore designed to correct the E-PT by considering the anatomical shape of the VPs (i.e. for eccentric VPs). This first step in improving E-PT was applied to coronary lesions of patients imaged *in vivo* with IVUS. Our preliminary results (Fig. 5) were promising, since we demonstrated that our original PALPO technique was more accurate than E-PT and was able to correct for the bias induced by the anatomical shape of the VP. This work is still in progress to capture and to correct also for the anatomical shapes of plaque inclusions present in VPs.

In 2013 also, we successfully developed and **patented** a new material-finite element formulation (named I-FEM) for the direct resolution of the inverse problem in elasticity (*Bouvier 2013*). An iterative finite element (FE) elasticity reconstruction method using strain measurements has been previously implemented by our group (*Le Floc'h 2009*). Although this approach could resolve the mechanical characterization of VPs, it suffers from major limitations since **(i)** it is not adapted to characterize VPs exhibiting high material discontinuities between inclusions, and **(ii)** does not permit real time elasticity reconstruction for clinical use. We therefore designed a direct **material-FE** algorithm for elasticity reconstruction problems which accounts for material heterogeneities. We originally modified and adapted the extended FE method (Xfem), used mainly in crack analysis, to model material heterogeneities (Fig. 6). This new algorithm was applied to coronary lesions of patients imaged *in vivo* with intravascular ultrasound. The results demonstrated the performance of I-FEM when considering accurate measurements of all strain components (see *Bouvier 2013*). However, the proposed elasticity reconstruction technique *I-FEM* appears to be very sensitive to noise in the strain measurements. Such result was expected since the proposed algorithm is linear. To overcome such limitation, we are currently developing relevant strain-noise filters and specific elasticity constraints.

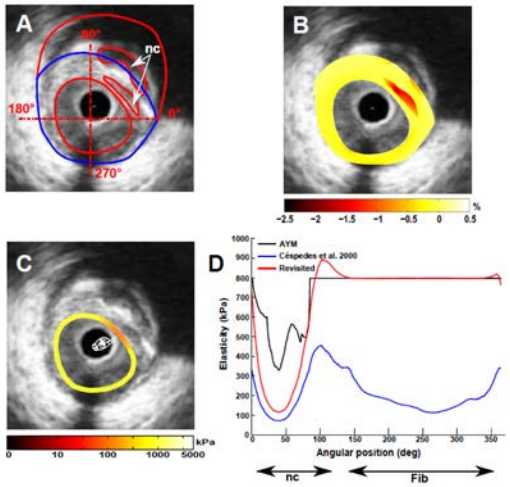

FIGURE 5. Performance of the improved elasticity-palpography technique to detect a vulnerable plaque with two necrotic cores. A) IVUS image of plaque # 4 with plaque constituents (red contours, "nc": necrotic core; "fi": fibrous region). The boundaries of the palpography domain Ω_{palpo} are also given (blue contours). B) Radial strain-elastogram in the palpography domain. C) Computed improved stress-strain modulus (S-SM) palpogram. D) Comparisons between native S-SM of Céspedes et al. (2000), improved revisited S-SM and averaged Young's modulus (AYM corresponding to the exact solution) palpograms. (from *Deleaval 2013 and Patent PALPO 2013*).

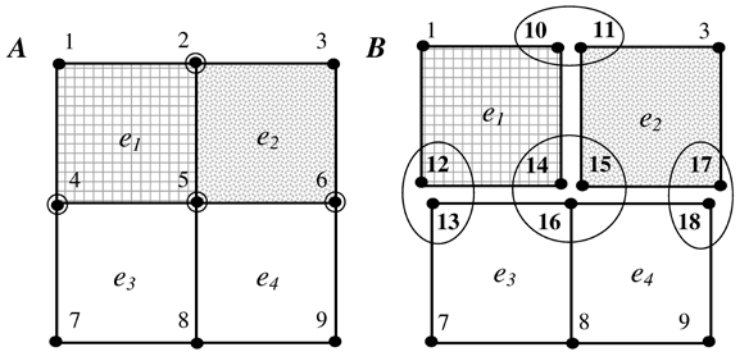

FIGURE 6. A) Regular mesh used for the finite element approximations of displacements and forces. B) Mesh used for the finite element approximation of material properties. Nodes located at the lines of material discontinuities (i.e. nodes # 2, 4, 5 and 6 of mesh A) were enriched and replaced by the following sets of nodes (10, 11), (12, 13), (14, 15, 16) and (17, 18), respectively. The three media were illustrated by distinct colors. The circled nodes are the enriched nodes. e_i (i=1 to 4) is the element number *i*. (from *Bouvier 2013 and Patent I-FEM 2013*).

BIBLIOGRAPHY

Baldewsing RA, et al. *Ultrasound Med Biol*, vol. 32, pp. 201-210, 2006 - Baldewsing RA, et al. Adv Cardiol, vol. 44, pp. 35-61, 2007 - Bouvier A, Ohayon J, et al. Phys Med Biol., (in press), 2013 - Broisat A, Ohayon J, et al. Arterioscler Thromb Vasc Biol, 31(5):1007-10 , 2011 - Céspedes et al. Ultrasound Med Biol, 26:385-96, 2000 - Chatzizisis YS, et al. J Am. Coll Cardiol, 49:2379-93, 2007 - Choudhury RP, et al. Nat Rev Drug Discov., 3(11):913-25, 2004 - de Korte CL, et al. Eur Heart J, vol. 23, pp. 405-13, 2002 - Deleaval F, Ohayon J, et al. Ultrasound Med Biol, 39:1469-81, 2013 - Dolbow J, et al. International Journal of Solids and Structures, 37(48-50) :7161-7183, 2000 - Doyley MM. Phys Med Biol 57(3):R35-73, 2012 - Eckel RH, et al. Lancet, 22;365(9468):1415-28, 2005 - Farb AP, et al. Circulation, 93:1354-63, 1996 - Fayad ZA, et al. Circulation, 106:2026-34, 2002 - Finet G, Ohayon J, et al. Coron Artery Dis, 15:13-20, 2004 - Fleg G, Ohayon J, et al. J Am. Coll Cardiol, Cardiov Imaging, 9:941-955, 2012 - Granada JF and Feinstein SB. Nat Clin Pract Cardiovasc Med, 5:S18-S25, 2008 - Hayenga HN, et al. J Vasc Res, 48:495–504, 2011 - Holzapfel GA, et al. American Journal of Physiology, 289:H2048-2058, 2005 - Kanai H, et al. Circulation, 107(24):3018-3021, 2003 - Khalil AS, et al. Cardiovasc Eng, 6:93-102, 2006 - Kim K, et al. Ultrasound Med Biol, 30:761-71, 2004 - Kotys MS, Ohayon J et al. Magnetic Resonance in Medicine, 62(2):292-99, 2009 - Kubo T, et al. J Am. Coll Cardiol, 50:933-939, 2007 - Le Floc'h S, Ohayon J, et al. IEEE Transactions on Medical Imaging, 28:1126-37, 2009 - Le Floc'h S, Ohayon J, et al. Phys Med Biol., 55(19):5701-21, 2010 - Le Floc'h S, Ohayon J, et al. Ultrasound Med Biol, (in press), 2012 - Lehoux S, Tedgui A. Hypertension, 32:338-345, 1998 - Lehoux S, et al. J Intern Med., 259:381-392, 2006 - Loyd-Jones D, et al. Circulation, 119 :480-486, 2009 - Luo J, et al. Ultrasonics, 44:e195-e198, 2006 - Maldonado N, et al. American Journal of Physiology, 303(5):H619-28, 2012 - Malvè M, Ohayon J, et al., Euromech 529, Cardiovascular Fluid Mechanics Cagliari-Italy, June 2011 - Maurice RL, Ohayon J, et al. J Acoust Soc Am. 116:1276-1286, 2004a - Maurice RL, Ohayon J, et al. IEEE Transactions on Medical Imaging. 23:164-180, 2004b - Mercure E, Ohayon J, et al. Comput Med Imaging Graph, (Special Issue, in press), 2013 - Naghavi M, et al. Circulation. 108:1664-1672, 2003 - Nandalur KR, et al. American Journal of Roentgenology, 184:295-298, 2005 - Nicolaides A, et al. International Angiology, vol. 22 pp. 263-272, 2003 - Ohayon J, et al. Coron Artery Dis, 12:655-63, 2001 - Ohayon J, et al. American Journal of Physiology, 293:H1987-1996, 2007 - Ohayon J, et al. American Journal of Physiology, 295:H717-727, 2008 - Ohayon J, et al. American Journal of Physiology, 301:H1097-1097, 2010 - Ohayon J, et al. Biomech Model Mechaniobiol, 11(6):801-13, 2012 - Ohayon J, et al. Ann Biomed Eng, (Special Issue, in press), 2013 - Riou L, Ohayon J, et al. J of Biomech, (Special Issue, in press), 2013 - Rioufol G, et al. Circulation, 106(7):804-8, 2002 - Roger VL, et al. Circulation, 125:e2-e220, 2012 - Soualmi L, et al. Presented at Acoustical Imaging, New York, Plenum, pp :203-209, 1997 - Stone GW, et al. N Engl J Med, 364(3):226-35, 2011 - Thim T, et al., Circ Cardiovasc Imaging, 3:384-391, 2010 - Tracqui P, Ohayon J, et al. J. Structural Biology, 174:115-123, 2011 - Van Mieghem CA, et al. J Am Coll Cardiol, 47(6):1134-42, 2006 - Vengrenyuk S., et al. Proc Natl Acad Sci, 103(40):14678-83, 2006 - Virmani R, et al. Arterioscler Thromb Vasc Biol 20: 1262-1275, 2000 - Yoshifumi S, et al. Ultrasonics, 44:e51-e55, 2006.