BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Elisa E. Konofagou

eRA COMMONS USER NAME (credential, e.g., agency login): EK2191

POSITION TITLE: Professor of Biomedical Engineering and Radiology

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Universite de Paris 6, Paris France	B.S.	06/1992	Chemical Physics
Imperial College, University of London, U.K.	M.S.	10/1993	Biomedical Engineering
University of Houston and University of Texas Medical School, Houston, TX	Ph.D.	08/1999	Biomedical Engineering
Brigham and Women's Hospital, Harvard Medical School, Boston, MA	Postdoctoral	09/2003	Therapeutic Ultrasound

A. Personal statement

I have been working in the area of FUS for opening the blood-brain barrier for over 14 years and have built a group of 12 people that are working on all aspects of the problem including ultrasound pulse optimization, microbubble dependence mechanism analysis, histology analysis, MRI imaging, fluorescence imaging, intravenous and intraperitoneal administration of compounds and transducer and setup designs for large animal and clinical use. For the purpose of this project, the therapeutic envelope of FUS for drug delivery as it pertains to early-stage Parkinson's in mice, NHP and humans that we have been working on over the past funding period. Building a team around us at Columbia, we will be able to implement a novel technology that integrates FUS with neuronavigation for flexibility in applying brain drug delivery for Parkinson's treatment reliably without the need for application inside a MRI system.

1. Choi JJ, Selert K, Vlachos F, Wong A, Konofagou EE. Noninvasive and localized neuronal delivery using short ultrasonic pulses and microbubbles. Proceedings of the National Academy of Sciences of the United States of America. 2011;108(40):16539-44. PMC3189054.
2. Wu SY, Sanchez CS, Samiotaki G, Buch A, Ferrera VP, Konofagou EE. Characterizing Focused-Ultrasound Mediated Drug Delivery to the Heterogeneous Primate Brain In Vivo with Acoustic Monitoring. Scientific reports. 2016;6:37094. PMC5112571.
3. Samiotaki G, Karakatsani ME, Buch A, Papadopoulos S, Wu SY, Jambawalikar S, Konofagou EE. Pharmacokinetic analysis and drug delivery efficiency of the focused ultrasound-induced blood-brain barrier opening in non-human primates. Magn Reson Imaging. 2017;37:273-81. PMC5316348.
4. Karakatsani ME, Samiotaki G, Downs M, Ferrera V, Konofagou E.Targeting Effects on the Volume of the Focused Ultrasound Induced Blood-Brain Barrier Opening in Non-Human Primates in vivo. IEEE Trans Ultrason Ferroelectr Freq Control. 2017 Mar 13. PMC5542068.

B. Positions and Honors

Positions and Employment

1993-1994 Research Assistant, National Center for Scientific Research (N.C.S.R.) Demokritos, Greece
1993-1994 Biomedical Engineer, Onassis Cardiac Surgery Center, Athens, Greece
1994-1999 Research Assistant, University of Texas Medical School-Houston, Houston, Texas
1999-2002 Research Fellow, Brigham and Women's Hospital, Harvard Medical School, Boston, MA
2002-2003 Instructor, Brigham and Women's Hospital, Harvard Medical School, Boston, MA

2003-2004 Visiting Scientist, Brigham and Women's Hospital, Harvard Medical School, Boston, MA
2003-2009 Assistant Professor of Biomedical Engineering and Radiology, Columbia University, New York, NY
2009-2010 Associate Professor (untenured) of Biomedical Engineering and Radiology, Columbia University, New York, NY
2010-2013 Associate Professor (tenured) of Biomedical Engineering and Radiology, Columbia University, New York, NY
2014-2016 Professor of Biomedical Engineering and Radiology, Columbia University, New York, NY
2016- Robert and Margaret Hariri Professor of Biomedical Engineering and Professor of Radiology, Columbia University, New York, NY

Other Experience and Professional Memberships and Study Section service

-American Association for the Advancement of Science
-American Institute of Ultrasound in Medicine
-Acoustical Society of America
-IEEE Society for Ultrasonics, Ferroelectrics and Frequency Control
-IEEE in Engineering in Medicine and Biology
-Ad hoc NIH Study Section Reviewer: National Institute of Deafness and Other Communication Disorders (NIDCD) panel, June 2008, NCRR Biotechnology Review Panel, October 2008, ZGM1 Scope of Competitive Research Award Panel, January 2009;, Bioengineering Research Partnership Review Panel, 2009/10 ZRG1 SBIB-V (50) R; Challenge Grants, RFA OD-09-003 Challenge 2009/10 ZRG1 SBIB-V (58) R, July 2009; Fellowship Review Panel, 2009/10 ZRG1 f15-l (20) l; Ultrasound Exploratory Panel, ZRG1, Oct. 2009;Fellowship Panel, ZRG1 2010/05 ZRG1 F15-D (20) L meeting, Feb. 2010, BTSS Feb. 2016, Quantum June 2016; Brain Intiative ZRG1 May 2017.
-Chartered NIH Study Section Reviewer: Biomedical Imaging Technology panel (BMIT-B), 2010-2014.
-Chartered NIH Study Section Reviewer: Biomedical Imaging Technology panel (MEDI), 2017-2021.

Honors

1994-1999 University of Texas Medical School-Houston, Graduate fellowship
1997 Hellenic Professional Society of Texas Scholarship
1999 Graduate Student Achievement Award, Sigma Xi competition - UH chapter
1999 RWB Stephens Student prize, World Conference in Ultrasound '99, Copenhagen, Denmark
2000 Award for the Best Non-Clinical Paper published in the journal of Ultrasound in Medicine and Biology in 1998 from the World Federation of Ultrasound in Medicine and Biology
2002 Young Investigator Award, Acoustical Society of America
2003 New Investigator Award (finalist), World Federation for Ultrasound in Medicine and Biology, Montreal, Canada
2004 American Heart Association Scientist Development Award
2005 Wallace H. Coulter Early Career Development Award
2006 New Investigator Award winner, American Institute of Ultrasound in Medicine, Washington, DC
2006 Press release selection out of 1,000 abstracts, Acoustical Society of America, Providence, RI
2006 Nominated for the 2006 World Technology Award in ‘Health and Medicine’, 2006 World Technology Summit, San Francisco, CA, Nov. 2006.
2006 Nominated for the Presidential Early Career Award in Science and Engineering (PECASE) by the National Institutes of Health (NIH).
2007 NSF CAREER Award recipient and nominated for the Presidential Early Career Award in Science and Engineering (PECASE) by the National Science Foundation (NSF).
2007 Nagy Award by the National Institute of Biomedical Imaging and Bioengineeiring (NIBIB) – NIH.
2008 Columbia University Diversity Initiative Award
2009 New Investigator Award winner, American Institute of Ultrasound in Medicine, New York, NY (with PhD student Wei-Ning Lee)
2009 International Society of Therapeutic Ultrasound Early Career Award
2011 Invited Participant, Frontiers of Engineering, National Academy of Engineering, San Francisco, CA
2012 Elected member, Board of Governors, American Institute of Ultrasound in Medicine (AIUM)
2014 Fellow, American Institute for Medical and Biological Engineering (AIMBE)
2014 Biomedical Wellness Pioneer Award, SPIE Defense, Security, and Sensing (DSS) Meeting

2014 Invited Moderator and Organizer, Biomedical Imaging Session, Japan-USA Frontiers of Engineering (JAFOE), National Academy of Engineering, Tokyo, Japan.
2014 Award for Best Paper published in the *Artery Research* journal (with Danial Shahmirzadi)
2014 Award for Best Paper published in the *Artery Research* journal (with Danial Shahmirzadi)
2015 Honored Paper in Computers in Biology and Medicine (with Jean Provost)
2017 Elected Fellow, Acoustical Society of America
2017 Bodossaki Foundation Prize for Scientific Excellence in Applied Science

C. Contribution to Science
(Total Peer-Reviewed-179; Orig. Articles-311; Abstracts-455; Book Chap.-15; Invited Articles-16)

Characterization of the mechanism of opening the blood-brain barrier with FUS
My laboratory has identified the mechanism of opening the blood-brain barrier (BBB) in mice and non-human primates by developing real-time cavitation devices that can detect microbubble activity through the intact skull. We have also shown that the BBB can open at low MI which makes it very safe to use in primates. We have verified the safety by testing for BBB closing or reversibility which happens within hours or days depending on the pulse length and pressure.

1. Tung YS, Marquet F, Teichert T, Ferrera V, Konofagou EE. Feasibility of noninvasive cavitation-guided blood-brain barrier opening using focused ultrasound and microbubbles in nonhuman primates. Applied Physics Letters. 2011;98(16):163704. PMC3094460.
2. Downs ME, Teichert T, Buch A, Karakatsani ME, Sierra C, Chen S, Konofagou EE and Ferrera VP (2017), Toward a Cognitive Neural Prosthesis Using Focused Ultrasound. Front. Neurosci. 11:607. PMC5694829
3. Tung YS, Vlachos F, Feshitan JA, Borden MA, Konofagou EE. The mechanism of interaction between focused ultrasound and microbubbles in blood-brain barrier opening in mice. The Journal of the Acoustical Society of America. 2011;130(5):3059-67. PMC3248062.
4. Samiotaki G, Vlachos F, Tung YS, Konofagou EE. A quantitative pressure and microbubble-size dependence study of focused ultrasound-induced blood-brain barrier opening reversibility in vivo using MRI. Magnetic resonance in medicine. 2012;67(3):769-77. PMC3658823.

Drug Delivery through the opened blood-brain barrier with FUS
We were the first to show that the neurotrophic factors can permeate through the opened BBB and trigger downstream signaling in neurons that are essential for neuroprotection and neuroregeneration. We also showed that the microbubble size can determine the extent of the BBB opening volume giving us for the first time control over what has been opened in the brain. My lab determined that the stiffness of these size-isolated bubbles differs which explains why the larger sizes are easier to open with (lower stiffness) than the smaller ones. In order to better facilitate transport and persistence, my group has also used nanodroplets that convert to microbubbles once activated by FUS that were also shown to induce opening at lower thresholds and more safely.

5. Baseri B, Choi JJ, Deffieux T, Samiotaki G, Tung YS, Olumolade O, Small SA, Morrison B, Konofagou EE. Activation of signaling pathways following localized delivery of systemically administered neurotrophic factors across the blood-brain barrier using focused ultrasound and microbubbles. Physics in medicine and biology. 2012;57(7):N65-81. PMC3919955.
6. Konofagou EE, Tung YS, Choi J, Deffieux T, Baseri B, Vlachos F. Ultrasound-induced blood-brain barrier opening. Current pharmaceutical biotechnology. 2012;13(7):1332-45. PMCID: PMC4038976.
7. Konofagou EE. Optimization of the ultrasound-induced blood-brain barrier opening. Theranostics. 2012;2(12):1223-37. PMC3563154.
8. Wang S, Kugelman T, Buch A, Herman M, Han Y, Karakatsani ME, Hussaini SA, Duff K, Konofagou EE., Non-invasive, Focused Ultrasound-Facilitated Gene Delivery for Optogenetics, Scientific Reports 7:39955, 2017. PMC5216389.

Parametric assessment of through the opened blood-brain barrier with FUS
My lab discovered that the pulse length and pressure can determine the permeability of the barrier and the duration of the BBB opening. We also showed that polydisperse bubbles are more efficacious and can open the barrier using stable cavitation as opposed to the commercially used bubbles such as Definity. The pressure was proven a major factor for larger size molecules and the higher the pressure, the larger the

molecules that permeate it. Finally, we have shown that both Adenoviral Vectors (AAV) and Neurturin triggers neurotrophic effects in mice.

9. Wang S, Samiotaki G, Olumolade O, Feshitan JA, Konofagou EE. Microbubble type and distribution dependence of focused ultrasound-induced blood-brain barrier opening. Ultrasound in medicine & biology. 2014;40(1):130-7. PMC3893303.
10. Chen H, Konofagou EE. The size of blood-brain barrier opening induced by focused ultrasound is dictated by the acoustic pressure. Journal of cerebral blood flow and. 2014;34(7):1197-204. PMC4083385.
11. Wang S, Olumolade O, Sun T, Samiotaki G, Konofagou EE. Non-invasive, neuron-specific gene therapy can be facilitated by focused ultrasound and recombinant adeno-associated virus, Gene Therapy 2015 Jan;22(1):104-10. PMC4294560.
12. Samiotaki, G., Acosta C., Wang S. and Konofagou, E**,** Enhanced Delivery and Bioeffects of the Neurturin (NTN) Neurotrophic Factor through Focused Ultrasound – Mediated Blood-Brain Barrier Opening in vivo, J. Cereb. Flow and Metab., 2015;35(4):611-22. PMC4420879.

List of Recently Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/elisa.konofagou.1/bibliography/40517030/public/?sort=date&direction=ascending

D. Research Support.

Ongoing Research Support:

R01 AG038961 (Konofagou) 08/01/2011-02/28/2021
NIH/NIA
Assessment of ultrasound-facilitated neurotherapeutics in Alzheimer's Disease
The main goal of this project is to determine the efficacy of delivery through the ultrasound-opened blood-brain barrier.

R01 HL140646 (Konofagou) 12/15/2017-11/30/2021
NIH/NHLBI
Arrhythmia mapping using electromechanical wave imaging.
Our objective is to develop a novel imaging methodology that can better identify arrhythmic origins and focally guide subsequent treatment so as to increase the current success rates and reduce the lengthy procedure times.

R01MH112142 (Ferrera; Konofagou) 04/01/2017-03/31/2022
NIH/NIMH
Focused ultrasound for noninvasive brain stimulation
The goal of this project is to test the efficacy of focused ultrasound for noninvasive brain stimulation and targeted drug delivery. Focused ultrasound could provide a new research tool for establishing causal brain-behavior relationships, mapping neural circuits in healthy humans, and a novel method for introducing neuroactive drugs that do no cross the intact blood-brain barrier (BBB).

R01HL135734 (Konofagou) 04/01/2017-03/31/2022
NIH/NHLBI
Carotid plaque assessment using Pulse Wave Imaging
This study aims at developing quantitative, contrast-free, non-ionizing and noninvasive assessment of atherosclerotic plaque stability or vulnerability that can be integrated into existing ultrasound scanners such as those routinely being wheeled to the bedside in noninvasive or interventional radiology or emergency rooms.

R01CA228275-01A1 (Konofagou) 06/11/2018-05/31/2023
NIH/NCI
An integrated theranostic system for breast cancer
The overall objective of this project is to integrate real-time elasticity-based monitoring into a clinical therapeutic ultrasound system. Such a reliable monitoring technique could prove pivotal in rendering an entirely noninvasive treatment accessible to a wide population of breast cancer patients for the first time by propelling it into fast and reliable outpatient procedure for the focal treatment of benign or small, non-metastatic breast cancer, thus minimizing mortality and risk.

R01EB0257576-01A1 (Konofagou) 04/04/2019-12/31/2022
NIH/NIMH
Mechanistic Monitoring of Ultrasound Neuromodulation
In this study, we will develop novel tools for improvement of focused ultrasound by monitoring its physiological and physical effects on the brain in real time.

1UG3NS115598-01 (Leong) 09/01/2019-07/31/2022
NINDS/NIH
Focused Ultrasound-mediated Delivery of Gene-editing Elements to the Brain for Neurodegenerative Disorders
The objective of this proposal is to develop a FUS-mediated technology for delivering AAV vector and nonviral delivery system carrying CRISPR elements to the brain and establish the efficacy on Alzheimer's and Parkinson's diseases in the murine and non-human primate models.
Role: Co-I

R01 EB006042 (Konofagou) 08/01/2010-05/31/2019
NIH/NIBIB [No cost extension 5/31/2020]
Early Detection and Mapping of Ischemia using Myocardial Elastography
The main goal of this project is to develop a myocardial strain imaging technique to detect onset of coronary artery disease at its early onset.

R01 EB029338 (Konofagou) 03/01/2020-12/31/2023
NIH/NIBIB
A theranostic system for ultrasound-facilitated blood-brain barrier opening
This study aims to develop a theranostic ultrasound system that can use a diagnostic transducer to open the blood-brain barrier noninvasively and selectively in order to facilitate gene delivery.

Completed Research Support:

BAA-15-06 ElectRx (Konofagou) 09/28/2015-09/27/2019
DARPA
PULSE: Phased-array ULtraSound for Electroceuticals
In this study, we perform integrated sensor design, biophysical modeling, animal and human studies for noninvasive ultrasound-based neuromodulation, and using intrinsically scalable technology.

R01 EB009041 (Konofagou) 09/30/2008-03/31/2018
NIH/NIBIB [No cost extension 3/31/19]
Optimization of Ultrasound-Facilitated Blood-Brain barrier Opening
The main goal of this technique is to determine the mechanism by which the blood-brain barrier opens and the role that the injected microbubbles play in determining the properties of the opened region.

R21 EB021103 (Konofagou) 01/01/2016-12/31/2018
NIH/NIHBIB
Intranasal delivery through the blood-brain barrier using focused ultrasound
In this study, We propose to develop an entirely noninvasive approach for trans-BBB deliver that offers the advantages of an injection-free approach, reduced systemic toxicity , reduced side-effects, reduced administered drug dose, lower cost, as well as, higher percentage of volume administered reaching the brain.

R01 HL114358 (Konofagou) 04/16/2013-01/31/2018
NIH/NHLBI
Noninvasive arrhythmia mapping using Electromechanical Wave Imaging
The main goal of this project is to develop one transthoracic and one intracardiac Electromechanical Wave Imaging system for mapping of atrial and ventricular arrhythmias in the clinic.

OVERLAP:

None.