

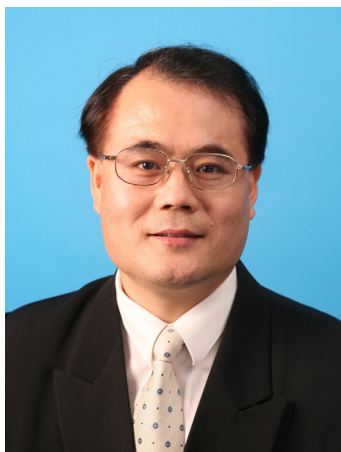
ACOUSTICAL NEWS—USA

Elaine Moran

Acoustical Society of America, Suite 1NO1, 2 Huntington Quadrangle, Melville, NY 11747-4502

Editor's Note: Readers of this journal are encouraged to submit news items on awards, appointments, and other activities about themselves or their colleagues. Deadline dates for news and notices are 2 months prior to publication.

New Fellows of the Acoustical Society of America



Li Cheng—For contributions to vibroacoustic modeling of complex structures



M. Patrick Feeney—For contributions to clinical middle-ear function through wideband reflectance



Philip Joris—For contributions to neural encoding in binaural hearing



Michael V. Scanlon—For contributions to the development of systems to detect and localize transient sounds in air



Michel Versiluis—For contributions to high speed imaging of time scale acoustic phenomena

Report of the 34th F. V. Hunt Postdoctoral Fellow, 2011–2012

James J. Choi

*Biomedical Ultrasonics, Biotherapy, and Biopharmaceuticals Laboratory
University of Oxford, Oxford, United Kingdom, OX3 7DQ*

It has been a great pleasure and honor to have worked as a Frederick V. Hunt Postdoctoral Research Fellow under the mentorship of Professor Constantin-C. Coussios at the University of Oxford. The broad scope of my research is to create incision-less surgical and drug delivery devices using ultrasound. In these techniques, a focused transducer generates ultrasound,

which propagates through skin and organs and converges to a small diseased volume, thus leaving the surrounding tissue unharmed. Yet the non-invasive ability of ultrasound, which makes this technology clinically attractive (e.g., infection-free, pain-less, etc.), has also made it difficult to study and control as the therapeutic activity occurs in deep and inaccessible regions. The Hunt fellowship funded my research to develop “acoustic vision” to enable the spatial, temporal, spectral, and quantitative imaging of ultrasonically generated activity deep within our body. With this technology, I have worked on numerous projects to both study the behavior of ultrasonic phenomena and develop methods to improve therapeutic capabilities.

The central acoustic phenomenon in my research is acoustic cavitation—acoustically driven bubble activity—which can be used as

microscopic sites of thermal or mechanical activity. By designing ultrasonic parameters to drive cavitation nuclei, either endogenous to our body or artificially engineered (e.g., microbubbles or solid hydrophobic particles), a wide range of effects may be produced. Stable cavitation—the expansion and contraction of a bubble—can alter vessel permeability or open pores in cell membranes. Inertial cavitation—the unstable expansion of the bubble followed by a violent collapse due to the inertia of the surrounding media—has been associated with vessel rupture and rapid heat generation.

In therapeutic applications, microbubbles, which are small enough to circulate throughout our extensive network of microvessels, are typically injected intravenously and subsequently sonicated. I created a controlled environment by flowing microbubbles through a vessel in a tissue-mimicking material (TMM). Upon sonication, the microbubbles radiated harmonic or broadband acoustic emissions, indicating stable or inertial cavitation, respectively. These emissions were captured using a sensor array and, with the passive acoustic mapping (PAM) algorithm, enabled characterization of cavitation dynamics (e.g., type, magnitude, distribution, and duration). At low ultrasonic pressures, stable cavitation could be maintained throughout a long pulse while being predictably distributed according to the shape of the ultrasonic focal volume. At high pressures, inertial cavitation dominated, but persisted for only 6–7 ms as microbubbles were rapidly destroyed. Interestingly, cavitation became progressively spatially biased upstream as it evolved during the pulse, thus showing a shift in the treated region. Multiple pulses emitted at rates below a flow-dependent critical rate produced predictable and consistent cavitation dynamics. Above the critical rate, energy generated was unpredictable and spatially biased. My analysis provided new insight into the relationship between pulse shape and sequence with cavitation dynamics and the *in vivo* biological environment, which both helped explain ultrasonic bio-effects observed empirically and provided a basis for optimizing pulse designs for future applications.

I then employed acoustic cavitation in mice to locally trigger the release of drugs from capsules (e.g., liposomes), open vessels of the tumor to allow drug transfer from blood to tissue, and enhance drug penetration deep into the tumor's tissue microenvironment. To this end, several challenges needed to be overcome: the tumor microvascular environments are animal-, organ-, and disease-specific and therefore unpredictable, ultrasonically driven cavitation activity remains poorly understood *in vivo*, and rapid tumor growth rates make comprehensive tumor coverage essential for successful therapy. In my work, PAM was employed to monitor ultrasound therapy and assess treatment success. Solid breast cancer tumors in mice were exposed to ultrasound following injection of microbubbles and a therapeutic agent, either self-replicating cancer-targeting viruses or cavitation-sensitive capsules containing drugs. Many characteristics of the cavitation dynamics observed in the tumor were similar to what was observed in the TMM. However, distinct from the TMM study, was the inhomogeneous and unpredictable spatial distribution of cavitation activity at the first pulse, which was likely due to the tumor's vascular inhomogeneity. In addition, ultrasonic pulses required emission rates to be below 1 Hz in order to produce therapeutically relevant levels of cavitation activity. I was also able to correlate the location of inertial cavitation activity to the location of drug release from the capsules. Thus, by mechanistically understanding cavitation dynamics *in vivo* and mapping the treatment distribution, I was able to optimize the efficiency and efficacy of delivering a cancer-targeting virus to tumors. My treatment resulted in inhibition of tumor growth rates and an increase in mouse survival.

I am grateful to the Hunt family and the Acoustical Society of America for the opportunity to contribute what I hope to be impactful findings to the scientific and engineering community. My experience has been an enjoyable and stimulating experience, having engaged a challenging problem and collaborated with excellent scientists at the University of Oxford. I am deeply indebted for the support and guidance, both personal and professional, by Prof. Constantin-C. Coussios. I am also grateful for faculty members including Dr. Robert Carlisle, Prof. Robin Cleveland, Dr. Eleanor Stride, and Prof. Len Seymour; post-doctoral scientists including Dr. Jamie Collin, Dr. Carl Jensen, Dr. Eleonora Mylonopoulou, Dr. Christian Coviello, Dr. Miriam Bazan-Peregrino, and Dr. Stephane Labouret; graduate students, including Dr. David Holroyd, Dr. Daniel Chung, Susan Graham, Joshua Owen, Sunali Bhatnagar, Liza Leung, Evelyn Buchner Santos, Edward Jackson, Graciela Mohamedi, Bassel Rifai, and Michael Molinari; and the entire Biomedical Ultrasonics, Biotherapy, and Biopharmaceuticals Laboratory.

The following publications and presentations resulted from my Hunt Fellowship:

Journal Publications—Published or Submitted

1. J. J. Choi and C. C. Coussios, "Spatiotemporal evolution of cavitation dynamics exhibited by flowing microbubbles during ultrasound exposure," *J Acoust Soc Am.* **132**(5), 3538–3549 (2012).
2. R. C. Carlisle, J. J. Choi, L. W. Seymour, and C. C. Coussios, "Enhanced viral activity in tumors using focused ultrasound and microbubbles—A long term study," in review (2012).
3. M. Bazan-Peregrino, B. Rifai, R. C. Carlisle, J. J. Choi, C. Arvanitis, L. W. Seymour, and C. C. Coussios, "Cavitation-enhanced delivery of a replicating oncolytic adenovirus to tumors by ultrasound," in review (2012).

Conference Presentations—Presented in Person

1. J. J. Choi, R. C. Carlisle, L. W. Seymour, and C. C. Coussios, "*In vivo* spatial correlation of cavitation activity to drug release in murine tumors," *IEEE International Ultrasonics Symposium*, Dresden, Germany (October 7–10, 2012).
2. J. J. Choi, R. C. Carlisle, L. W. Seymour, and C. C. Coussios, "Passive acoustic mapping during cavitation-enhanced virotherapy *in vivo*," *12th International Symposium on Therapeutic Ultrasound*, Heidelberg, Germany (June 10–13, 2012).
3. J. J. Choi, R. C. Carlisle, L. W. Seymour, and C. C. Coussios, "Inhibition of tumour growth through focused ultrasound and cavitation-enhanced delivery of polymer-coated oncolytic adenovirus," *UK Therapy Ultrasound Interest Group*, London, Great Britain (Feb. 13, 2012).
4. J. J. Choi, and C. C. Coussios, "Spatio-temporal mapping and characterization of acoustic cavitation seeded by microbubbles and solid microparticles during focused ultrasound exposure," *Acoustical Society of America Meeting*, San Diego, CA, USA (October, 2011).
5. J. J. Choi, R. C. Carlisle, and C. C. Coussios, "Enhanced viral activity in tumors using focused ultrasound and microbubbles—a long term study," *Acoustical Society of America Meeting*, San Diego, CA, USA (October, 2011).

ADVANCED-DEGREE DISSERTATIONS IN ACOUSTICS

Editor's Note: Abstracts of Doctoral and Master's theses will be welcomed at all times. Please note that they must be limited to 200 words, must include the appropriate PACS classification numbers, and formatted as shown below. If sent by postal mail, note that they must be double spaced. The address for obtaining a copy of the thesis is helpful. Submit abstracts to: Acoustical Society of America, Thesis Abstracts, Suite 1N01, 2 Huntington Quadrangle, Melville, NY 11747-4502, e-mail: asa@aip.org.

Individualized Binaural Technology (Subtitle: Measurement, Equalization and Perceptual Evaluation) [66.Pn, .66.Qp, 60.Dh]—

Bruno Sanches Masiero, Institute of Technical Acoustics (ITA), RWTH Aachen University, Neustrasse 50, 52056, Aachen, Germany; bma@akustik.rwth-aachen.de. December 2012 (Ph.D.).

In this work the importance of individualization in binaural technique is investigated. The results extend the present knowledge on the efficient measurement of individual head-related transfer functions (HRTFs) and highlight the importance of individual equalization filters in binaural reproduction, using both loudspeakers and headphones.

An innovative measurement setup is developed to allow the fast acquisition of individual HRTFs. The hardware is designed to be compatible with the range extrapolation technique. An individual HRTF dataset with 4000 directions can be measured in less than 6 min with this new setup. Further, a framework is presented that integrates causality constraints to the regularized frequency domain calculation of crosstalk cancellation (CTC) filters. This framework also addresses the switching of active loudspeakers applying a weighted filter calculation method. A sound localization test showed that individualized CTC systems provide performance similar to that of binaural listening while nonindividualized CTC systems provide a significantly lower localization performance. Finally, a robust individual headphone equalization method is proposed. Perceptual tests showed that, in all but one of the tested situations, no audible differences between the original sound source and its binaural auditory display could be perceived. Publisher: Logos Verlag Berlin, 2012; ISBN:978-3-8325-3274-1.

Advisor: Michael Vorländer

Calendar of Meetings and Congresses

Based on the calendar compiled by the Information Service of the International Commission for Acoustics

2013			
15–17 March	Merano, Italy EAA Winter School http://www.aia-daga.eu.html	11–16 August	Budapest, Hungary, Third International Conference on Effects of Noise on Aquatic Life http://www.an2013.org/
17–20 March	Les Arcs, France Electroceramics for End-users VII (PIEZO 2013) http://www.piezoinstitute.com	26–28 August	Denver, USA NOISE-CON 13 http://www.inceusa.org
17–22 March	Les Houches, France http://houches.ujf-grenoble.fr/	27–30 August	Denver, USA Wind Turbine Noise 2013 http://www.inceusa.org
18–21 March	Merano, Italy AIA-DAGA 2013/EAA EUROREGIO http://www.aia-daga.eu	04–06 September	Portoroz, Slovenia 12th International Conference “Application of Contemporary Non-destructive testing in Engineering” (ICNDT 2013) http://lab.fs.uni-lj.si
23–25 April	Marrakech, Morocco 1st Euro-Mediterranean Conference on Structural Dynamic and Vibroacoustics (MEDYNA 2013) http://www.medyna2013.com	08–13 September	Pirenopolis, Brazil International Bioacoustics Congress (IBAC 2013) http://www.ibacbrasil.com/Home.html
1–4 May	Singapore 3rd International Congress on Ultrasonics (ICU 2013) concurrently organized with the 32nd International Symposium on Acoustical Imaging (AI 2013) http://www.epc.com.sg/ICU2010.pdf	15–18 September	Innsbruck, Austria Internoise 2013 http://www.internoise2013.com
20–23 May	Hong Kong 2nd Symposium on Fluid-Structure-Sound Interactions and Control http://www.fssic2013.com/	23–27 September	San Diego, CA, IEEE Oceans 2013 http://www.oceans13mtsiesandiego.org/
26–31 May	Vancouver, Canada 2013 IEEE International Conference on Acoustics, Speech and Signal Processing (ICASSP) http://www.icassp2013.com	7–9 October	Bloomington, IN, Aging and Speech Communication: An Interdisciplinary Research Conference
02–07 June	Montreal, Canada 21st International Congress on Acoustics (ICA 2013), 165th Meeting of the Acoustical Society of America, and 52th Annual Meeting of the Canadian Acoustical Association http://www.ica2013montreal.org	9–11 October	Hangzhou, China 4th Pacific Rim Underwater Acoustics Conference (PRUAC 2013) http://pruac.zju.edu.cn/index.htm
04 June	Montreal, Canada, Sound in the Sea: Recent Discoveries and Applications http://www.dosits.org	2–6 December	San Francisco, USA 166th Meeting of the Acoustical Society of America http://www.acousticalsociety.org
09–11 June	Toronto, Canada International Symposium on Room Acoustics (ISRA 2013) http://www.isra2013.com	2014	
10–13 June	Bergen, Norway, Oceans’13 http://www.oceansconference.org/	7–10 April	OCEANS’14, Taipei, Taiwan http://www.oceansconference.org/
12–15 June	St. Andrews, Scotland, 6th International Workshop on Detection, Classification, Localization and Density Estimation of Marine Mammals using Passive Acoustics http://soi.st-andrews.ac.uk/dclde2013/	5–9 May	Providence, USA 167th Meeting of the Acoustical Society of America http://www.acousticalsociety.org
17–21 June	Moscow, Russia, Ocean Acoustic Interference Phenomena rouseff@apl.washington.edu	06–10 July	Beijing, China 21th International Congress on Sound and Vibration (ICSV21)
23–28 June	Corfu, Greece 5 th International Conference on Underwater Acoustics Measurements: Technologies and Results http://www.uam-conferences.org	07–12 September	Krakow, Poland Forum Acusticum 2014 http://www.fa2014.pl/
07–11 July	Bangkok, Thailand 20th International Congress on Sound and Vibration (ICSV20) http://www.icsv20.org	14–19 September	St. John’s, Newfoundland, Canada, OCEANS’14 http://www.oceansconference.org/
23–26 July	Glasgow, UK Invertebrate Sound and Vibration (ISV 2013) http://www.isv2013.org	06–10 October	Prague, Czech Republic 11th European Conference on Non Destructive Testing http://www.ecndt2014.com/
30 July–03 August	Stockholm, Sweden Stockholm Music Acoustics Conference (SMAC 2013) http://www.european-acoustics.org/smac-2013	27–31 October	Indianapolis, USA 168th Meeting of the Acoustical Society of America http://www.acousticalsociety.org
		16–19 November	Melbourne, Australia Internoise 2014 http://www.internoise2014.org
		2015	
		11–15 May	Metz, France 4th International Congress on Ultrasonics (ICU 2015) http://www.me.gatech.edu/2015-ICU-Metz/
		18–22 May	Pittsburgh, USA 169th Meeting of the Acoustical Society of America http://www.acousticalsociety.org
		19–21 May	OCEANS’15, Genoa, Italy http://www.oceansconference.org/
		2–6 November	Jacksonville, USA 170th Meeting of the Acoustical Society of America http://www.acousticalsociety.org
		2016	
		05–09 September	Buenos Aires, Argentina 22nd International Congress on Acoustics (ICA 2016) http://www.ica2016.org.ar/