Conversation with a Colleague: Eleanor Stride

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Meet Eleanor Stride

Eleanor Stride is the next acoustician in our "Sound Perspectives" series "Conversation with a Colleague." Eleanor is currently a professor of bioengineering at Oxford University, United Kingdom, specializing in stimuli-responsive drug delivery. She obtained her BEng and PhD from University College London (UCL), United Kingdom, before moving to Oxford in 2011. She has over 200 publications and 12 patents and is a director of two spin-out companies set up to translate her research into clinical practice. She is a Fellow of the Acoustical Society of America (ASA), The Institute of Engineering and Technology (IET), and the Royal Academy of Engineering. She was elected as an Honorary Fellow of the Electrical Research Association (ERA) Foundation for contributions to public engagement. She received the ASA Bruce Lindsay Award and the IET A. F. Harvey Prize, was nominated as 1 of the 100 most influential women in engineering in 2019, and was made an Officer of the Order of the British Empire in 2021. Outside of work, she is a passionate dancer and teaches Lindy Hop and other swing dances. We asked Eleanor to give us her elevator pitch and then to elaborate on her inspirations, contributions, and hopes for the future.

Give your "elevator speech" about the thrust(s) of your scholarly work over your career.

There have been amazing advances in the development of new drugs over the twentieth and twenty-first centuries, yet millions of people still die every year from heart disease, cancer, and infection. There are many reasons for this, but one important factor is that there has been surprisingly little attention given as to how the drugs are delivered. Most drugs are given by mouth or by injection. The problem with that is that they go everywhere in the body and a very small percentage goes to the disease site. The rest is at best flushed out of the body and at worst leads to major side effects. The aim of my research is to try to tackle this lack of accurate targeting. My team are therefore developing ultrasound-responsive micro- and nanoparticles to encapsulate drugs so that they don't interact with tissue until they reach the target site. We try to get as many particles as possible in the target region, for example, by making the particles magnetic or attaching molecules to their surfaces that bind to particular types of cells. We then use a short burst of ultrasound focused on the target region to trigger the release of the drug.

What inspired you to work in this area of scholarship?

The short answer is a series of lucky coincidences. I pursued a very mixed set of subjects at my high school in London: mathematics, physics, and chemistry together with Latin, art, and general studies. I was always much happier solving mathematics and physics problems than writing essays, but I did also much enjoy the opportunities for independence and creativity offered by art. It was actually art that led me to engineering. When I was 16, my art teacher took me to the end-of-year exhibition by postgraduate students on the industrial design course at the Royal College of Art in London. Seeing the amazing work on display made me determined to pursue a career as an industrial design engineer, and three years later I enrolled as an undergraduate in mechanical engineering at UCL. After university, I intended to take a postgraduate course in industrial design. During the

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final year of my degree, however, I worked on a research project developing an experimental rig and software for imaging inside an oil pipe using ultrasound. I very much enjoyed the project and also became fascinated with ultrasound physics. A serendipitous meeting with a senior radiologist at UCL Hospitals then introduced me to the amazing properties of microbubbles and their potential use in both ultrasound imaging and therapy. It was this that led me to pursue my PhD and subsequently a research fellowship. I have been playing with bubbles and other types of particles ever since.

Of all your contributions during your career, which are you most proud of and why?

That is a very hard question to answer because almost everything in my research is linked to something else, so picking out just one bit is very difficult. Also, almost of my work is collaborative and involves lots of people from different disciplines. Thus, I never really feel that anything is "mine." It is always my team's contribution. I am still very excited by a project that I started during my research fellowship on creating magnetic microbubbles. I still remember when I first saw the magnetic bubbles move under the microscope when I brought a magnet close to them. I could not believe that the idea had actually worked.

I was even more excited to subsequently collaborate with a cancer biologist to see if we could use the magnetic bubbles to increase the efficiency of ultrasound-mediated gene transfer. It had already been shown in the literature that exposing cells to microbubbles and ultrasound in the presence of DNA could push DNA into the cells. The cells would then express the relevant gene. The efficiency of the transfer process was, however, very low. Our idea was to place a magnet under the lower surface of the plate on which the cells were growing. The magnet would pull the magnetic bubbles down toward the cells and this would increase the probability of a microbubble being in contact with a cell membrane when we turned on the ultrasound. Hence the probability of the bubble being able to transfer DNA into the cell would hopefully increase. The experiments did not get off to a great start. It was my first experience of working with cells, and on the first go I managed to kill everything. I was so worried about keeping everything sterile that I used double-distilled water instead of saline, thinking it would be "cleaner," but, unfortunately, distilled water is lethal for cells. Luckily, things went a lot better after that, and we saw a fourfold increase in gene expression with the magnetic bubbles compared with a commercial microbubble agent.

That project has evolved considerably and, in addition to improving the microbubble formulation substantially, we have developed a new type of ultrasound probe that incorporates a magnetic array so we can do simultaneous imaging and targeted therapy (for more on this, please see bit.ly/AT-Gray). We have had some very promising results in both cancer models and for delivering anticlotting agents for stroke therapy. Yet it has been challenging to move the technology toward clinical application because it is such a big change compared with current procedures, but we are getting there slowly.

Another extremely exciting moment was the first time we saw a beneficial effect in a human volunteer. This was for a study using bubbles to try to boost oxygen levels in tissue. I was absolutely terrified something might go wrong, even though we had tested everything very carefully in the laboratory, including in mice, and I had even taken some of the oxygen bubbles myself just to be sure. When we saw the oxygen levels go up in the first volunteer and there were no side effects, we were all jumping around in excitement. We have gone on to do three more studies in humans. Two of these have been in sets of healthy volunteers, and one in a group of patients. So far, the results have been encouraging, and we are hoping this will enable us to develop new treatments for a range of conditions including lung disease and cancer.

If I do have to pick one contribution, then I would probably choose our work on cancer. One of the reasons for developing the oxygen bubbles is that many cancerous tumors have very low levels of dissolved oxygen and that makes them very resistant to almost every type of treatment. My colleagues John Callan and Tony McHale at Ulster University in Northern Ireland have been working on a novel type of therapy using ultrasound-activated drugs to treat pancreatic cancer. Unfortunately, these drugs are very ineffective in the absence of oxygen. John and Tony approached me at a conference to ask if it was possible to tag their drugs onto oxygen-loaded

bubbles, and the project grew from there. We have now taken the bubbles into production in a clean room facility and are hoping to run our first clinical trial next year. Pancreatic cancer remains one of the most lethal forms of cancer, and survival rates have not improved since the 1960s. We are hoping that we will be able to change that. The project has also led to some extremely interesting fundamental science on the mechanisms by which the drugs are activated by ultrasound. These mechanisms are very far from understood.

What are some of the other areas in which you feel you made substantive contributions over your career?

Something I have started to care about enormously as I have gone further in my career is public engagement. I get very upset when I hear colleagues dismissing public engagement as "soft" and not real work. There is a terrible problem with a lack of understanding and hence a lack of trust of science and technology among the general public and, sadly, also among politicians and journalists. An obvious example is the resistance to vaccination that became so acute during the Covid-19 pandemic. I find this very bizarre and distressing because most people's lives are dependent on technology in some form or another. I think it is vital that scientists and engineers do everything we can to combat that lack of trust in science and to do that, we need to communicate regularly, clearly, and honestly about what we do, including the many things we just do not know. I have contributed to quite a few TV and radio programs and also several podcasts and videos (see bit.ly/CWC-Stride1; bit.ly/CWC-Stride2; bit.ly/CwC-Stride4; bit.ly/CwC-Stride5; bit.ly/CwC-Stride6). Initially, I was absolutely amazed that anyone downloaded them, but the feedback has been great, particularly from high-school students. Indeed, I was at an event recently and a lady came up to me and said: "You don't know me, but our physics teacher showed us your video at school and that's why I did physics at university and am now doing a PhD." Possibly the most important and humbling engagement I am involved in is working with patient groups. I think that understanding what they are experiencing and what they value and need is absolutely vital if one is working in biomedical engineering.

What do you think are the most pressing open questions that you would like to focus on over the next 5-10 years?

My immediate priorities are the work we are doing on cancer and also our using microbubbles for the delivery of antibiotics to treat drug-resistant infection. We are hoping to run clinical studies in both these applications in the near future. There are, however, many interesting questions in terms of the fundamental science that my team is working on as well. It's becoming increasingly evident that when we use ultrasound and bubbles to deliver drugs in one part of the body that we are also triggering system-wide effects, in particular an immune response. Understanding that and how we can control it is crucial to ensure patient safety. It is also potentially a response that could be usefully exploited such as to prevent cancer from coming back after therapy.

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