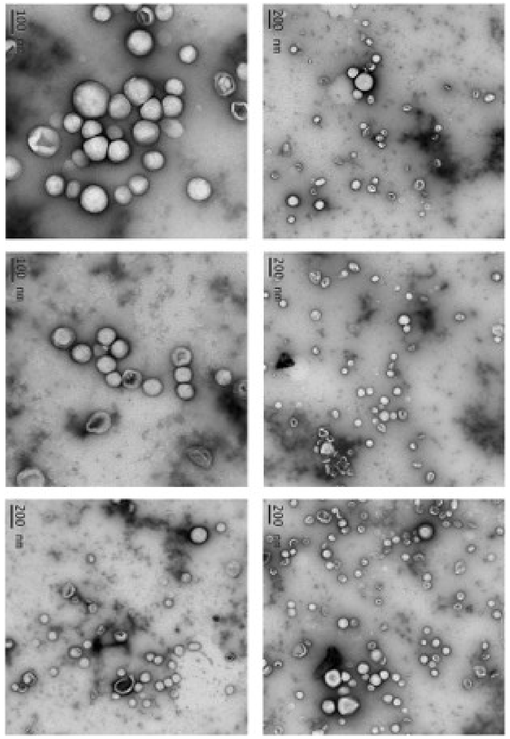

Image credit: University of Leeds

Engineering and Physical Sciences Research Council

Developing New Therapies: Case Study

Microbubbles aim for major impact in tackling cancer

Better targeting of tumours, reductions in dosages of toxic drugs, fewer debilitating side-effects: an ingenious technique combining innovative 'microbubbles' with tried-and-tested ultrasound technology could trigger a step forward in the battle against cancer.

Meeting the Grand Challenge:

Led by the University of Leeds, the 'Microbubble-enhanced Imaging and Therapeutic Delivery' project has driven forward a pioneering approach to delivering drugs to exactly where they are needed in the human body. Based on specially designed bubbles just a micron or two wide, this technique aims to transform the treatment of colorectal cancer and, potentially, other cancer types and a whole range of infectious diseases. It can also be adapted to make diagnosis quicker and easier.

Vision and Value:

Every year in the UK, colorectal cancer – the third most common type in this country – causes around 17,000 deaths, with case numbers rising due to an ageing population. Drugs used to treat the condition are generally highly toxic and, while some of the active ingredients reach the cancer, the rest dissipate around the body. This results in unwelcome side-effects throughout the course of a treatment programme.

The Leeds team was driven by a vision of a drug delivery mechanism that minimised the amount of active ingredient spreading beyond the cancer. As well as dramatically cutting side-effects, this would mean the same efficacy could be achieved with a lower drug dosage or a higher level could be achieved with the same dosage as currently used. The mechanism's value would increase if it could also be harnessed as a diagnostic tool.

Key Components:

Supported by a £835,000 EPSRC Standard Research grantand due to end in 2021, the four-year project has interwoven physics and engineering, augmented by clinical expertise to help define and develop the translation pathway for the new technique. Alongside project partners the Medicines Discovery Catapult and the University of Bradford, the Leeds team has progressed the technique – which had achieved proof-of-concept in a previous EPSRC-funded project – to the point where it is now ready for clinical trials.

The concept centres on microscopic bubbles consisting of a lipid shell surrounding a gas core. Tiny drug capsules can be attached to the shell, together with an antibody to help the target the drugto the cancer. Capable of going wherever red blood cells go, the microbubbles 'look' like cells to the body's immune system so do not trigger an immune response. After injection, ultrasound is used to track their progress and, when they reach the cancer, a short, sharp increase in ultrasound level makes them burst and deliver the drug; this also punches holes in the cancer cells, helping the drug stick to them.

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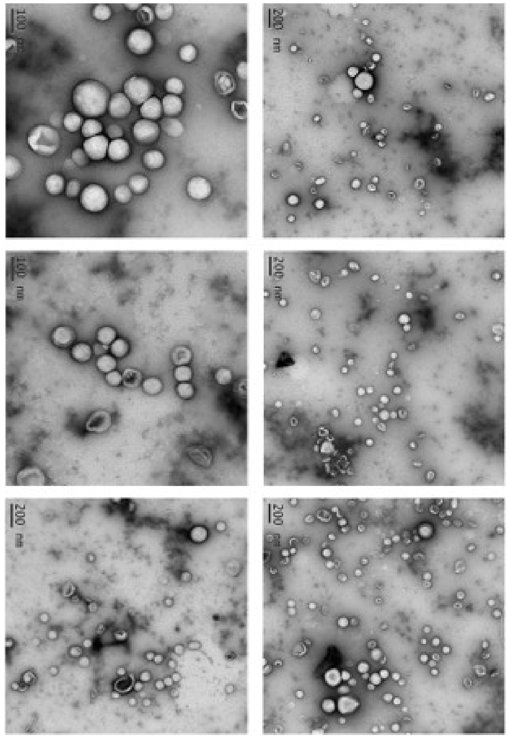

Image credit: University of Leeds

The microbubbles are fabricated using microfluidics chips made from standard polymers but specially modified to enable large numbers of microbubbles to be manufactured at once.

Outputs and Outcomes:

- The technique has been shown to be capable of achieving the same therapeutic impact using 40 times less of a drug.
- This team has demonstrated the practicality of freeze-drying drug-loaded microbubbles and restoring them simply by adding water and shaking, which is vital to real-world application as microbubbles typically only last a few hours.
- The microfluidic chip designs for bubble production have been patented and an Ultrasound Array Research Platform (UARP) has been developed at Leeds specifically to burst microbubbles using ultrasound.
- To date, the team has built seven microbubble-making instruments. The Medicines Discovery Catapult, The University of Edinburgh, Stanford University in the US and Erasmus Medical Centre in the Netherlands are each using one of these.
- Initial work on designing nanobubbles even smaller than the microbubbles, for insertion inside drugs to target hard-to-reach regions in the body, has produced promising results.

Impacts and Benefits:

- **More effective cancer care.** Better treatment and earlier diagnosis will not only save lives, they will also help reduce anxiety among those suffering, or suspected of suffering, from cancer.
- **Improved quality of life for patients.** Reducing side-effects resulting from cancer treatment could be life-changing for huge numbers of people and more effective treatment could also make fewer hospital trips necessary.
- **Savings in healthcare costs.** The potential to make courses of cancer treatment shorter but no less effective and to reduce the quantity of anti-cancer drugs used per patient could free-up healthcare resources for other purposes.
- **Better treatment of other diseases.** The new technique offers enormous scope for adaptation to other clinical uses besides cancer care, such as targeting places in the body suffering from bacterial infections.
- **Reduced resistance to antibiotics.** Achieving the same health outcomes with lower drug dosages has positive potential implications for the future of antibiotics and could be a valuable weapon against the growing threat of antimicrobial resistance.

Next Steps:

The team is exploring potential licensing arrangements and spinout possibilities and is in preliminary discussions with potential instrument manufacturers. Optimisation of the new technique is ongoing, with the aim of working towards clinical trials that can fully demonstrate its safety and efficacy, plus its economic and quality-of-life benefits. The team also plans to explore the prospects for adapting it for DNA or gene delivery.

Behind the Project:

Professor Steve Evans is the project's Principal Investigator. On this project, he has worked with a large, multidisciplinary team including eight Co-investigators at Leeds and one at both Bradford and the Catapult. "This is just part of a long-term plan designed to demonstrate microbubbles' therapeutic and diagnostic effectiveness and then translate them to clinical settings," Steve says. "A multidisciplinary team is absolutely critical to successfully tackling this sort of challenge."

46,000

cases of colorectal cancer are diagnosed in the UK each year

Relevant EPSRC Research Areas:

- Clinical Technologies
- Medical Imaging