Project Details	
Project Code	MRC22IIARBr Byrne
Title	Establishing Magnetic Nanoparticle Design Guidelines for Maximizing Clinical Efficacy
Research Theme	Infection, Immunity, Antimicrobial Resistance & Repair
Summary	Using nanotechnology in medicine has been widely discussed for several decades yet remains elusive due to questions surrounding effectivity, biocompatibility and in vivo clearance. Supervised across Universities of Bristol, Bath and Cardiff, this interdisciplinary project will develop design guidelines for customizing biocompatible magnetic nanoparticles based on the target clinical application such as magnetic hyperthermia and site-specific drug delivery.
Description	Magnetic nanoparticles (MNPs) are well suited to a range of targeted medical applications including hyperthermia cancer therapy, drug delivery, and magnetic resonance imaging (MRI). However, the physical requirements of the MNPs are often incompatible for different applications. For instance, whilst a heating response is required for magnetic hyperthermia applications, movement along a magnetic field gradient is necessary for targeted drug delivery. This project aims to address specific barriers to the clinical use of MNPs, by linking physicochemical properties of the MNPs to their magnetic response and hence therapeutic efficacy and thereby establishing guidelines for the custom design of MNPs as required for target application. Biogenic MNPs can be produced with controlled particle size, magnetisation, aggregation, and surface chemistry, which are critical in determining the effectiveness of MNPs. Furthermore, biogenic MNPs are typically coated in organic molecules which are essential for shielding the MNPs from the surrounding body and can promote sorption of drugs and other compounds. In contrast chemically synthesised MNPs do not have such coatings which must be added later. We can effectively customise biogenic MNPs using laboratory protocols developed by the PI (Byrne et al., Nanotechnology, 2011, Byrne et al., Advanced functional materials, 2014). Customising those physiochemical properties is essential for different applications, e.g., to enhance the temperature response for cancer hyperthermia (Moise et al., Nanoscale, 2018; Moise et al., Scientific Reports, 2017), or to incorporate fluorescent molecules for improving image contrasting. This project will combine the interdisciplinary expertise of three research groups to focus on fabricationand characterisation of MNPs (BYRNE); biocompatibility and screening of MNPs in vitro (MOISE); and in vivo in eye disease models (MEAD) through distinct, interrelated work packages (WP): WP1 – Mapping out MNP properties to the target clinical applications: This WP will generate a map linking the required features (drug/biomolecule binding capacity; evading the immune system) and magnetic properties MNPs (heating response; T1/T2 relaxation; motility along a field gradient) to different clinical applications including site-specific delivery, MRI imaging, hyperthermia as well as for combined theranostics. WP2 – Customisable MNP synthesis and characterisation: An array of MNPs will be produced through biogenic and abiogenic protocols with varying physiochemical properties. We will screen this array to link the effect of key physicochemical properties on the magnetic response and features

	of the MNPs. Specifically, we will measure the impact of core composition, core size, surface composition, hydrodynamic size, surface charge, magnetic relaxation mechanisms and link these to surface binding properties to different drug and biomolecules (proteins, nucleotides), specific loss power (heating capacity), etc. WP3 – Biocompatibility and efficacy: We will assess the biocompatibility and magnetic response within a biological milieu of the MNP array synthesised in WP2. We will assess the impact of the nanoparticles on cellular viability, proliferation, differentiation, metabolic activity using standard spectrofluorimetric and molecular biology techniques. In addition, we will assess the heating response, cellular uptake and delivery of biomolecule or drug cargo and the effectiveness of the therapeutic cargo on the cells using commercially purchased cell lines. Having identified the most promising candidates, their efficacy will be tested in the eye disease model available for the target clinical applications. The findings from this project will have play an important role in making critical progress towards realising the full potential of MNPs for clinical applications.
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