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Enhancement of microbubble mediated gene delivery by simultaneous exposure to ultrasonic and magnetic fields

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It has been shown in previous studies that ultrasound mediated gene delivery can be greatly enhanced by the presence of contrast agent microbubbles and that transfection efficiency is highly dependent upon both bubble/cell separation and the ultrasound field parameters. It has also been shown that gene delivery can be promoted by exposing cells to a magnetic field in the presence of DNA conjugated to magnetic nanoparticles. The aim of this work was to investigate whether it was possible to combine the advantages of both these techniques. It was found that transfection of Chinese hamster ovary cells by naked plasmid DNA was enhanced by simultaneous exposure to ultrasound (40-cycle sinusoidal pulses, centre frequency 0.5-3MHz, peak negative pressure 0.25-1.5MPa, repetition frequency 1kHz for 10s) and a uniform magnetic field (3-5Nm-3) in the presence of two different microbubble/nanoparticle preparations. The first consisted of phospholipid-coated microbubbles mixed with micelles containing magnetic nanoparticles; the second of microbubbles which were themselves magnetically active. These preparations were found to be much more effective than either magnetic micelles or phospholipid-coated microbubbles alone. The mechanisms underlying these observations in terms of microbubble dynamics, the sensitivity to the ultrasound parameters and their significance for potential therapeutic applications will be discussed.