Ultrasound-mediated Non-invasive Gene Transfer
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Introduction
As a result of its non-invasive nature, ultrasound as stimulus for gene transfer is emerging as a significant alternative to the use of viruses for such purposes [1]. Microbubble-based agents are employed to enhanced ultrasound-mediated gene transfer and because of their response to externally-applied ultrasonic fields, can provide significant opportunities for achieving site-specific gene transfer. Here we will present some of our work in this area and suggest potential applications of the technology in tissue engineering and regenerative medicine.

Materials and Methods
RIF-1 cells and C3H/HeN mice were employed as in vitro and in vivo targets, respectively. A Sonidel SP100® sonoporator was employed to generate ultrasound and the Sonidel MB101® microbubble was used to enhance gene transfer. Luciferase-encoding reporter plasmids were used to assess gene transfer and gene expression was detected by measuring bioluminescence.

Results
Initially gene transfer was performed in a 96-well plate configuration and this was found to be highly compatible with high throughput application. In order to demonstrate the site-specific nature of ultrasound-mediated gene transfer an Opticell®-based configuration was employed and data are shown in Fig. 1A below. The patterns of gene expression detected in plates indicate the high degree of spatial specificity achievable with this approach. In extrapolating the approach to demonstrate site-specific gene transfer and expression in vivo, plasmid DNA was injected into the hind-leg muscle of subjects and the site-specific nature of gene expression is shown in Fig.2. Apart from the intramuscular injection, this process was completely non-invasive.

Discussion and Conclusions
Ultrasound can be used to stimulate site-specific gene expression either in vitro or in vivo and the degree of non-invasive spatiotemporal control afforded by this technology offers significant potential in areas such as tissue engineering/regenerative medicine.

References

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Disclosures
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