INTRODUCTION

New diagnostic and treatment techniques for chronic lower back pain involve localized drug delivery into the lumbar intervertebral disc [1,2]. A better understanding of these new techniques could be gained by measuring drug concentration at specific intradiscal locations at different time points [1]. Currently, there are no established methods for quantifying real-time in situ drug concentrations in the human intervertebral disc; however, injection profiles have been successfully characterized in pig disc, human brain, adipose tissue, and blood using microdialysis [3,4,5]. This technique involves continuous sampling of interstitial fluid via semi-permeable membranes mounted on miniature, implantable catheters [6]. Given the success of the microdialysis technique in characterizing the real-time composition of other poroelastic tissues, we hypothesize that this method will be similarly successful when applied to human lumbar disc. Thus, the goal of this study was to evaluate the microdialysis method for characterizing intradiscal drug concentrations. For the purposes of this study, we used lidocaine (4% Roxane Laboratories Inc.), a common anesthetic, as the drug therapy of interest, and we conducted two separate experiments. First, benchtop tests were performed using known lidocaine concentrations to determine the appropriate flow rate and collection time for the microdialysis apparatus. Using these settings, the microdialysis technique was applied to cadaveric lumbar discs saturated in lidocaine to determine the relative recovery in situ [3,4].

METHODS

Benchtop tests were conducted as follows. Microdialysis probes (CMA-20, CMA Microdialysis, Inc.) were placed in microcentrifuge tubes containing a known amount of lidocaine, C_i (1 ng/mL – 1 mg/mL, diluted with 1x PBS) and connected to an adjustable flow rate pump (CMA-400, CMA Microdialysis, Inc.). For each concentration, flow rates and collection times were varied from 0.3-2.4 µL/min and 5-20 minutes, respectively. The initial solutions were not stirred or shaken to simulate conditions in the intervertebral disc.

In situ tests were conducted on fresh-frozen human lumbar intervertebral discs (N=2, Specimen 1: L4-L5 35/C/M; Specimen 2: L1-L2 58/C/M). Each specimen was immersed in a 0.1% lidocaine solution at 4°C for six days prior to microdialysis sampling. Microdialysis probes were inserted into the outer annulus and mid-nucleus, and samples were taken using the optimized settings determined from the benchtop experiments.

RESULTS

Samples collected during the benchtop experiments were sensitive to variance in flow rate and to a lesser degree in collection time (Figure 2). Based on these data, it was determined that for in vitro tests the relative recovery (C_o/C_i) of lidocaine was high when the flow rate was above 1µL/min. In situ, relative recovery in the annulus was 90.2±31.9% at 1µL/min and 53.3±16.2% at 0.6 µL/min (Specimen 1).

DISCUSSION

We found the microdialysis technique to be a promising method for detecting lidocaine in the human intervertebral disc after the tissue reached a steady-state saturation in lidocaine. Flow rate values from bench-top experiments had relative recoveries near 100%; however, when this flow rate was applied in situ, anesthetic recovery decreased for both the annulus and nucleus tissue. This may be explained by physical principles. Specifically, at higher microdialysis flow rates, the probes removed lidocaine from extracellular fluid faster than the rate of diffusion across tissue, resulting in a decrease in the measured concentration at longer collection times. While initially the higher flow rate had higher recovery, recovery was lower by the time the microdialysis catheter system reached equilibrium. At the lower flow rate the system achieved equilibrium very quickly but still suffered loss in collection due to the difference in diffusive properties between extracellular fluid and tissue [3]. However, this error was systemic and uniform across all collection times and a correction factor may therefore be applied to test samples to improve accuracy.

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REFERENCES