BIOSYSTEMS ENGINEERING 138 (2015) 59–64

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/issn/15375110

Special Issue: Innovations in Medicine and Healthcare

Research Paper

Effect of injection pressure and fluid volume and density on the jet dispersion pattern of needle-free injection devices

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ARTICLE INFO

Article history:
Published online 16 May 2015

Keywords:
Needle-free injection
Fluid dispersion
Ballistic gelatin
High-speed photography

Needle-free injection devices improve vaccinator safety and optimise vaccine delivery time by eliminating the use of needles involved with traditional vaccination techniques. Of significant importance is a full understanding of the relationships that exist between the injection properties and the depth and shape of the injectate's dispersion. Work has been done to characterise the distribution of human needle-free injection devices, but little research has been conducted on livestock injections, which operate at much higher pressures and volumes. Therefore, the aim of this research was to characterise the injection profile of a livestock needle-free injection device while varying the injection pressure and fluid volume and density. Water and porcine circovirus vaccine were injected into ballistic gelatin blocks and the injection mechanism was captured using high-speed photography. The volume was varied between 1.0 and 2.5 ml and orifice pressure between 40 and 220 MPa. It was found that pressure influenced the depth of penetration, but had little effect on the shape of the injection profile. In contrast, the volume and density increased the penetration depth and varied the dispersion pattern. These results can be used to better understand how the injection profile of a needle-free injection device changes given an initial set of parameters. This will be important for developing administration protocols that successfully deliver intradermal, subcutaneous, and intramuscular livestock injections.

1. Introduction

Needle-free injection devices (NFIDs) offer several advantages over conventional needle-syringe administration techniques. Vaccinator safety is greatly improved by eliminating the risk of accidental needle-stick injuries (Mitragotri, 2005) and vaccine efficacy is enhanced through greater tissue dispersion (Grosenbaugh, Leard, Pardo, Motes-Kreimeyer, & Royston, 2004). Although needle-free injection dates back to the 1930s (Mitragotri, 2006) there remains a fundamental lack of understanding of the mechanisms governing jet dispersion through skin and into subcutaneous tissue. Knowledge of fluid dispersion is key to optimising drug absorption and will aid in

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http://dx.doi.org/10.1016/j.biosystemseng.2015.04.010
1537-5110/

the development of more effective needle-free administration protocols.

NFIDs employ a high-velocity stream of liquid (~150 m s^{-1}) through a small orifice (~150 μm) penetrating skin and depositing fluid within tissue (Donnelly, Morrow, McCarron, Garland, & Woolfson, 2007). Intradermal, subcutaneous, and intramuscular injections can be administered by varying the velocity and/or diameter of the jet stream (Aguiar et al., 2001). However, a complete understanding of jet dispersion under various conditions is limited by the complexity of skin, which is non-homogenous, anisotropic, and opaque. Accordingly, models have been developed to analyse the dispersion of jet streams in soft materials including polyacrylamide gel (Baxter & Mitragotri, 2005; Schramm-Baxter, Katrencik, & Mitragotri, 2004) and silicon rubber (Shergold, Fleck, & King, 2006).

Previous studies have shown that jet penetration occurs in three distinct steps: erosion, stagnation, and dispersion (Schramm-Baxter & Mitragotri, 2004). A cylindrical hole is formed during erosion creating a pathway for the fluid to travel through the tissue. The fluid follows the path of least resistance and reaches a point of stagnation where it is dispersed into a bolus. Previous studies have described the shape of the dispersion pattern as an upper hemisphere, lower hemisphere, or ellipsoid (Figge & Barnett, 1948; Schramm-Baxter et al., 2004), cone shaped (Wagner, Dues, Sawitzky, Frey, & Christ, 2004), spider-web-like (Chase, Daniels, Garcia, Milward, & Nation, 2008), and fan shaped (Seyam et al., 1997).

Penetration of fluid into tissue is dependent on a number of variables including the jet velocity, orifice diameter, fluid volume and viscosity and material stiffness and porosity. Jet velocity and diameter have been shown to affect fluid penetration through a parabolic relationship (Schramm & Mitragotri, 2002) and fluid penetration increases linearly with increasing volumes (Donnelly et al., 2007). There exists a nonlinear relationship between the thickness of skin and the penetration depth (Baxter & Mitragotri, 2005) and increasing the viscosity leads to a shallower depth of penetration (Donnelly et al., 2007). However, these and other relationships have been derived from human NFIDs, which operate at much smaller doses and pressures than livestock injections. The jet mechanics involving large volumes and high pressures are yet to be characterised.

The objective of the present study was to analyse the jet mechanics of a livestock NFID under various injection pressures and fluid volumes and densities. Understanding the relationships that exist between the dispersion profile and the fluid and injection properties will be key to optimising needle-free administration to livestock.

2. Materials and methods

A commercially available AcuShot™ NFID (Fig. 1) was used to administer 1.0–2.5 ml injections at 40–220 MPa orifice pressures. The device was powered by a lithium polymer battery and nitrogen cylinders and had an orifice diameter of 300 μm. The reported pressures represent the average pressure at the start of injection. The injector supplied a constant volume, so the pressure decreased over the duration of the injection after the skin was broken.

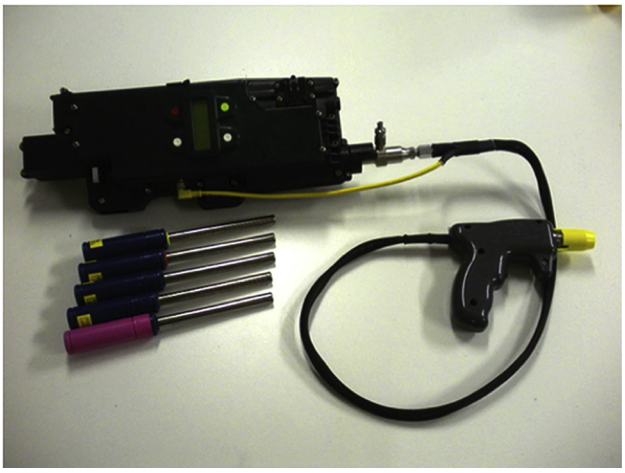

Fig. 1 – AcuShot™ needle-free injection device with five inert nitrogen power cylinders. Each cylinder is capable of administering injections at a predetermined pressure. The device is powered by a rechargeable lithium polymer battery and is able to control the volume and injection pressure administered to the injection medium.

Ballistic gelatin was chosen as the injection medium because of its transparency, which allowed for a real time analysis of jet mechanics through high-speed photography. A 10% per weight mixture of ballistic gelatin (Jussila, 2004) was prepared using 250 A bloom gelatin (Sigma Aldrich, USA). Briefly, 10% per weight gelatin powder was added to 40% per weight distilled water at 21 °C. The water-gelatin mixture was added to 50% per weight distilled water at 72 °C and stirred slowly for 10 min. The mixture reached a thick consistency and was added to 15 × 6 × 2 cm acrylic moulds and foam was removed from the surface of the fluid. The gelatin was incubated for 24 h at room temperature (23 °C) and then stored at 4 °C for an additional 24 h.

The force-displacement relationship of the gelatin moulds was characterised using a Ta.XT2i (Stable Microsystems, USA) texture analyser. A 12.6 mm diameter sharp edge plunger was used to compress the surface to 5 mm at a rate of 0.05 mm s^{-1}. The results were compared to force-displacement relationship of swine tissue from the shoulder of a market-ready sow.

Ballistic gelatin samples were placed on a stage 30 cm from a high-speed camera (Casio, USA) (Fig. 2). The NFID was used to administer deionised water (1.00 g ml^{-1} density) or porcine circovirus vaccine (PCV) (Pfizer, Canada) (1.36 g ml^{-1} density) into ballistic gelatin and images were captured at a rate of 60 fps using high-speed photography. Two drops of blue dye (Ateco, USA) were added to the fluid to enhance the contrast of the dispersion pattern. Five injections were administered to each gelatin block with spacing of 1 cm between injection sites. The NFID was activated by pressing the injector head onto the surface of the gelatin block, which triggered release of the injectate. Consequently, there was no standoff distance present between the injector and the gelatin throughout the administration. The force required to trigger the device was